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THE PRESENT TREND OF TRANSURETHRAL RESECTION

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CHICAGO

Eight years has elapsed since Davis [1] first presented his paper on resection before the annual meeting of the American Medical Association in 1932. During this time a voluminous literature has been built up that has dealt with all phases of the subject. Enough time, it would seem, has elapsed so that a summary of the present status of resection is in order; if further justification were needed for the summary, the undeniable fact that a complete change of view has been effected during this time should give us pause.

During the early phase of the subject many articles dealt with the reasons why the procedure could not withstand the test of time and why it was not a sound one. Gradually an increasing number of articles dealing with the bad functional results were written, and attention was called to the number of complications.

As one might reasonably expect with any new and highly technical procedure, complications due to technical difficulties were reported, such as injuries to the urethra with rupture and urinary extravasation, perforation of the bladder with injury to the rectum, injury to the intestine with peritonitis, retroperitoneal cellulitis and intravesical explosions.

As the technic of the procedure was mastered, with the possible technical complications constantly kept in mind and every attempt made to avoid them, the number of these complications was greatly reduced.

During the past few years the number of patients who suffer from coronary thrombosis, attacks of angina pectoris, hypotension and hypertension has practically doubled, a fact emphasized in a previous publication.[2] Since that time there has been no change in this trend, and as a matter of fact many of these cardiac patients are sent in with the specific request that their obstruction be relieved by resection.

Many of these patients because of their cardiac condition are very poor risks for any major operative procedure. Transurethral resection, with its absence of shock and lower operative mortality and with fewer postoperative complications, is easily the method of choice in the management of these bad cardiac cases. The following case is an illustration:

History.—C. M., aged 78, admitted to the Presbyterian Hospital Aug. 22, 1938, had had attacks of angina pectoris for twelve years. These attacks were characterized by severe precardial pain, with severe dyspnea. He stated that he had had at least 1,000 attacks of angina.

The prostatic symptoms began five years previously, and at this time he was advised not to have anything done because of the seriousness of his cardiac condition. His chief complaints were difficulty in starting the stream, terminal dribbling, incontinence, pain and burning on urination. The urinary symptoms gradually increased in severity, so that it was necessary for him to strain a good deal before starting the stream, and the straining frequently brought on an attack of angina pectoris.

Physical Examination.—He was well nourished and well developed. The head, neck and lungs were normal. Examination of the heart showed the borders slightly larger than normal, with no murmurs. The heart tones were faint, the rate and rhythm normal. The electrocardiogram showed myocardial damage. Rectal examination revealed benign enlargement of the prostate, grade 3 plus. There was 100 cc. of residual urine. Bilateral inguinal hernia was noted. The blood pressure was 166 systolic, 70 diastolic.

Laboratory Examination.—The urine contained no albumin, no sugar, no blood and no pus. The culture was sterile. The phenolsulfonphthalein test showed an output of 55 per cent in ninety minutes.

The blood count and blood chemistry were normal. The Kahn test was negative.

Operation.—A transurethral resection was carried out Aug. 23, 1938, under caudal anesthesia. Enough tissue was removed to pack tight a medicine glass. Microscopic examination showed benign hyperplasia of the prostate.

Postoperative Course.—After the resection the patient had a fever ranging from 100 to 101 F. for two days. The temperature was normal at the end of the second day. Convalescence was uneventful. The indwelling catheter was removed on the sixth postoperative day, and the patient was discharged on the ninth postoperative day.

With freedom from pain on urination and straining there has been marked reduction in both the number and the severity of his attacks of angina.

Examination Oct. 23, 1939, showed no residual urine.

Furthermore, the number of patients sent in for resection and the number who suffer from serious coexisting lesions also are on the increase. I refer to the patients who have had a resection of the rectum or colon for carcinoma, patients with metastatic carcinoma, patients with severe pulmonary lesions, such as marked emphysema, severe bronchitis and asthma, and patients with hemiplegia—a group of patients for whom the advantages of resection as against prostatectomy are of great importance.

Another definite trend at the present time is not to deny men in the older age group relief of their obstruction solely on the basis of their age. Because of the well recognized clinical fact that there is a very definite increase in operative mortality in each decade, men in the eighth and ninth decades were advised not to subject themselves to surgical prostatectomy.

With the advent of resection a definite trend away from this type of advice is obvious and men in these

Read before the Academy of Medicine, Toronto, March 5, 1940.

1. Davis, T. M.: Present Status of Prostate Obstruction, J. A. M. A. **99**: 1928 (Dec. 3) 1932.
2. Kretschmer, H. L.: Ann. Surg. **104**: 917 (Nov.) 1936.

age groups are advised to have a resection because of the lower mortality rate, so that one does not hesitate to relieve these patients irrespective of their age.

History.—J. D., aged 99, admitted to the Presbyterian Hospital March 26, 1938, had had urinary symptoms for four or five years. He complained of great frequency of urination, being obliged to void every thirty minutes during the day and every fifteen minutes during the night. There were severe dysuria, slowing of the stream and terminal dribbling. For the past eight months he was treated with testicular hormone, and as a result of this treatment his symptoms rapidly increased.

Physical Examination.—He was thin and poorly nourished and almost deaf. The head, neck and lungs were normal. The heart was enlarged to the left and the rate irregular; a loud systolic mitral murmur was heard at the apex. An electrocardiogram revealed an advanced coronary artery sclerosis. The blood pressure was 152 systolic, 70 diastolic. There was 60 cc. of residual urine.

Laboratory Examination.—Urinary albumin was reported 2 plus, blood 2 plus and pus 4 plus. Culture of the urine showed Bacillus coli. The phenolsulfonphthalein test showed an output of 75 per cent in ninety minutes. The Wassermann test was negative. The blood urea nitrogen was 28.4 mg. and nonprotein nitrogen 45 mg. Red blood cells numbered 3,600,000 and white blood cells 9,200, and the hemoglobin content was 72 per cent.

Roentgen Examination.—No stone appeared in the urinary tract. Intravenous pyelograms revealed a slightly dilated lower ureter on the right and a double pelvis on the left. A cystogram showed multiple diverticula.

Operations.—March 30, 1938, an electroresection of the prostate was carried out under caudal anesthesia. A half medicine glass of tissue was removed. The temperature returned to normal on the second postoperative day. Several examinations for residual urine revealed 60 cc. April 18 a second resection was performed, and enough tissue to fill three medicine glasses was removed. The microscopic diagnosis was benign hyperplasia of the prostate gland.

Postoperative Course.—After the second resection convalescence was smooth and uneventful. The catheter was removed on the second postoperative day, and on the seventh day the patient left the hospital.

Examination a year and a half later, when the patient was 101, was negative as there were no complaints on his part. Residual urine measured 10 cc.

Shortly after the inauguration of resection it was severely criticized because of some of the bad results which followed its use. The method was criticized without taking into consideration the man who sat at the other end of the resectoscope. The same criticisms might be made of any surgical procedure. Here, as in any other form of surgery, it must be recognized that criticism and evaluation of any new form of surgical treatment must take into consideration the surgeon who carries it out, his qualifications, training and aptitude, especially in a highly technical procedure such as resection.

For example, in one case the procedure was criticized because it failed to relieve the symptoms when as a matter of fact failure was due not to the method but to the fact that the operator removed only a small part of the obstruction and overlooked the presence of a large stone in the bladder. Removal of the stone and complete removal of the obstruction resulted in a cure.

History.—A. G., aged 53, admitted to the Presbyterian Hospital Sept. 12, 1939, had a transurethral resection performed elsewhere fourteen months before. He received no relief whatever from his symptoms. His complaints on admission were extreme frequency of urination both day and night so that he was obliged to void every half hour, slowing of the stream, terminal dribbling and great pain and burning during the act of micturition. He frequently noted blood in the urine.

Physical Examination.—He was emaciated and appeared to be ill. A number of furuncles were scattered over the body. The head, neck, heart, lungs, abdomen and external genitals were normal. The blood pressure was 140 systolic, 90 diastolic. On rectal examination the prostate was twice the normal size. There were no signs of carcinoma.

The blood count and blood chemistry were normal. Urinalysis showed albumin 4 plus and pus. Culture of the urine yielded short chain streptococci and B. coli. A catheter passed easily into the bladder; a sensation of grating was obtained, which was interpreted as being due to the presence of stone in the bladder.

Roentgen Examination.—A bladder stone the size of a peach appeared. Intravenous pyelograms were normal. A cystogram showed numerous small diverticula.

Operation.—Sept. 13, 1939, a suprapubic cystotomy was performed and the stone removed. The bladder was drained for ten days, and September 25 a transurethral resection was done under sacral anesthesia. Examination with the resectoscope revealed large middle, intra-urethral and intravesical lateral lobes. Two medicine glasses of tissue were removed. Histologic examination revealed benign hyperplasia.

During the postoperative course acute pyelitis developed and on the thirteenth day there was a secondary hemorrhage. The clots were evacuated with a Bigelow pump and the bleeding points fulgurated. Two days later he was given a blood transfusion of 500 cc. He was discharged October 1.

Examination on October 24 showed no urinary symptoms and there was no residual urine.

Clearly the persistence of symptoms following the first resection cannot be charged to the method as such.

It is very interesting to note that although this method was taken up with avidity in this country, in Europe the urologists looked somewhat askance at the procedure and for long were doubtful of its beneficial effects. Bruni,[3] in a recent publication, calls attention to this fact and asks "Could this have been due to faulty technic or imperfection of instruments?"

An interesting statement was made recently by Riba [4] with regard to the major points in the discussion. He said: "Considerable credit should be given to those who are well trained in open surgery but who for the benefit of the patients have pursued the transurethral method and mastered its technic."

The historical review of this subject, the development of the various types of instruments used, the advantages of this method, the necessity for careful preoperative study and preparation of the patient, the dangers and complications, all these important matters have been more or less expatiated on by many authors at various times; hence a repetition here of what has been written on the subject would be superfluous.

Whereas formerly there was much difference of opinion regarding the type of patient who should have a resection there is one definite common ground on which all urologists agree: Practically all believe that the small bars, contractures, small middle lobes and small intra-urethral lobes are best handled by resection, and most urologists agree that the carcinomatous prostate when it produces obstruction should be handled by resection. It goes without saying that a resection in cancer of the prostate is much to be preferred to a permanent suprapubic fistula, even if a second and third resection become necessary. Moreover, many patients who are afflicted with carcinoma of the prostate are seen so late in the course of the disease that only a small percentage are amenable to radical surgery.

3. Bruni, C.: J. belge d. urol. **11**: 78 (April) 1938.
4. Riba, L. W.: Internat. Abst. Surg. **68**: 74-92, 1939, in Surg., Gynec. & Obst., January 1939.

The only debatable point centers around the treatment of the large prostate. Here opinions still differ. On the one hand, the surgically minded have taken a definite stand that large prostates should be removed by open surgery, whereas many urologists believe that even very large prostates should be resected. This is a very debatable point since a prostate that has been diagnosed as being too large for resection by one physician, who says it must be removed by prostatectomy, is subsequently removed by resection by another. Another interesting fact is that as the experience of the operator increases, the number of his resections increases and the number of prostatectomies decreases, which is akin to stating that as one's experience increases the number of prostatectomies decreases because the proficiency of the operator permits him to resect the large prostates.

Whether or not resection will ever completely replace prostatectomy is open to question. In a previous publication I stated that in the fifty-one months prior to 1936 I had performed only one prostatectomy, all other patients having been treated by resection. Since this statement was made in 1936 I have performed one suprapubic prostatectomy and the reason I performed it was the fact that it was impossible to introduce the resectoscope. T. M. Davis is of the opinion that prostatectomies are mandatory in 2 per cent of the cases.

The question of whether or not the very large prostate should be treated by resection or prostatectomy may automatically solve itself, when in the future the patient with prostatism will seek relief early rather than late in the course of the disease, long before the prostate reaches an enormous size and prior to the onset of the severe distressing symptoms which occur late in the course of the disease.

Once he is aware of the fact that he may obtain relief by a method that has in its favor a low mortality rate, with a much shorter period of morbidity, with fewer and less serious complications and with good functional results, it is reasonable to assume that the prostatic patient of the future will seek relief early rather than late in the course of the disease.

Early relief of prostatic obstruction changes the clinical picture of obstruction as far as many of the associated pathologic conditions are concerned. The results of long-standing obstruction of the bladder neck are well known. At first they are mechanical, resulting in diverticula or diverticulosis, hydro-ureter and hydronephrosis; sooner or later infection is superimposed and cystitis, ureteritis, pyelonephritis and infected hydronephrosis result. If the obstruction continues, renal atrophy with impaired renal function occurs, and finally uremia and death of the patient. Stone formation in the bladder and upper tract may occur, either before or after infection is added to the results of urinary obstruction.

If patients are treated early, the entire clinical picture is changed because these complications will not occur. Here as in other fields of surgery, the undeniable importance of early relief of obstruction is written large. In view of the fact that the late effects of obstruction are well known and have been known from time immemorial, that they can be prevented, and that when present they increase the mortality rate, it is difficult to understand the advice so often given a patient that an early operation is not necessary but that by watchful waiting, followed by an operation, many points will be gained.

Whereas formerly indications and contraindications were rather rigid, during the past few years a good many urologists have become more liberal in selecting cases for resection. This liberalization applies especially to the patient with impaired renal function. If after careful preliminary study and after instituting adequate drainage and treatment the blood chemistry studies show relatively high values, resection is carried out; it should be borne in mind that as a result of the long-standing obstruction, a certain amount of renal damage that is irreparable has taken place and because of this the function will never return to normal.

As one's experience with resections increases, resections are carried out in the presence of larger amounts of residual urine without preliminary catheter drainage, or with shorter periods of drainage. Thus at the present time resection is done without preliminary drainage in the presence of 6, 7 or even 8 ounces of residual urine provided the renal function is good, the urine grossly clear and the heart and lungs in good condition.

These remarks, however, are not to be misconstrued and to be interpreted to mean that one should dispense with careful preliminary study and preparation. What I attempted to state was that a good many urologists have liberalized their own personal indications and contraindications based on their personal experience.

When resection was introduced a good many preliminary cystostomies were done, and some urologists advised this as a routine before doing a resection. I have never subscribed to this procedure but have used preliminary drainage in the cases of very bad infection and in the presence of large or multiple stones. In other words, I weighed the pros and cons carefully with regard to the cases in which a preliminary cystostomy was indicated.

During the past few years the number of preliminary cystostomies indicated has become less and less. This may partly be explained because of increased experience, but the major reason is that the patients seek relief earlier (encouraged by the results of resection) and thereby reduce the number of bad infections.

In this connection it might be well to discuss a small group of patients who have marked urinary symptoms, whose prostates are small or normal in size on rectal examination and who have a small amount of residual urine. It is perhaps this group to whom the criticism is directed that many patients are being subjected to resection who should not be operated on at all. They might well be classified as on the borderline; hence at times it may be extremely difficult to make a decision. Under these circumstances, I institute a course of local treatment—namely, sitz baths or heat by rectum, massage, instillations and the internal use of sedatives such as hyoscyamus and bromides. If this regimen should fail to relieve the patient I advise a resection. In this group of patients the rectal examination may show the prostate normal or only slightly enlarged, whereas the instrumental examination shows the presence of well marked intra-urethral protrusion of the lateral lobes.

The present status of the treatment of diverticula associated with prostatic obstruction is a matter that should invite discussion. Whereas in the days of suprapubic and perineal prostatectomy all diverticula were removed, at the present time there is a very definite tendency not to remove them as a routine procedure. As a matter of fact, I no longer perform routine diverticulectomies.

In discussing the treatment of diverticula, it is necessary to assume that the obstruction at the bladder neck has been removed completely. It is well known

that if the obstruction has been completely removed, many diverticula tend to decrease in size and produce no subjective symptoms. The question as to whether the diverticulum or diverticula should be removed will depend on several factors and demands individualization.

1. *Small Diverticula.*—I do not remove small diverticula if the obstruction is removed completely, the urine is clear and subjective symptoms are absent.

2. *Larger Diverticula.*—Here again, if the obstruction has been completely removed, if the patient is free of symptoms, if the urine is clear or slightly hazy owing to bacteria and contains a few pus cells, and if the diverticulum is not close to the ureter so as to produce ureteral obstruction, I am of the opinion that administering urinary antiseptics and keeping the patient under close observation is all that is necessary.

However, if the ureter is obstructed, the pyuria does not clear up and there are recurring attacks of chills and fever, accompanied with urinary symptoms, or if the diverticulum does not empty, I believe the patient should have a diverticulectomy.

3. *The Very Large Diverticula.*—Here of course one must take into consideration the size and number of the diverticula, whether or not there are manifestations of peridiverticulitis, whether or not the diverticulum retains urine and hence is a source of infection, the amount of infection in the urine and the relation of the ureter to the diverticulum. As a rule, I remove the large diverticula first and then perform the resection.

During the early days of resection, most urologists were satisfied to remove just enough tissue to make a channel through the prostatic urethra. It soon became evident that this procedure was not sufficient and that a larger amount of tissue must be removed. Some, if not a good many, of the early patients who subsequently required a second resection undoubtedly belong to the group who had an insufficient amount of tissue removed. However, as one's experience with this method grows, more and more tissue is removed, and many urologists are of the opinion that the whole prostate should be removed. With this view I am in complete accord and I believe the term transurethral prostatectomy would be justified.

TABLE 1.—*Amounts of Residual Urine in First Group of 273 Patients Tested After Transurethral Resection*

Amount	Cases	
	Number	Per Cent
No residual	181	66.30
11-20 cc.	44	16.11
Total 82.41 per cent		
21-30 cc.	17	6.22
31-40 cc.	5	1.83
41-50 cc.	6	2.19
Over 50 cc.	20	7.32

As has been previously mentioned the objective of the treatment of prostatic obstruction, whether by perineal or suprapubic or by transurethral resection, is to remove the obstruction completely, and if the obstruction has been completely removed a cure will result. Whether or not the obstruction has been completely removed can best be determined by demonstrating the presence or absence of residual urine. It seems to me that this is a very critical evaluation of the result obtained.

If one method is just as effective as the other in relieving the obstruction completely, if it carries with it a lower rate of morbidity and mortality, and if it can be used in patients who are "poor surgical risks," then it seems to me that that particular operative procedure should be the one of choice.

TABLE 2.—*Amounts of Residual Urine in Second Group of 273 Patients Tested After Transurethral Resection*

Amount	Cases	
	Number	Per Cent
No residual	207	75.82
11-20 cc.	33	12.08
Total 87.90 per cent		
21-30 cc.	19	6.95
31-40 cc.	2	0.73
41-50 cc.	2	0.73
Over 50 cc.	10	3.75

It might be well to call attention to the fact that small amounts of residual urine present at the time the patient is discharged from the hospital gradually disappear. Even large amounts of urine tend to disappear completely, provided the obstruction has been completely removed. When large amounts of residual urine persist for more than a few weeks after resection and when repeated examinations show that the obstruction has been removed, one naturally becomes interested in determining the cause of the large residual. In this type of case one's attention is naturally turned toward the possibility of lesions of the central nervous system or to the possibility of muscular atony.[1]

If the patient suffers from some lesion of the central nervous system that was recognized before the resection, the question naturally arises with regard to the possible role that it might play, and hence another neurologic study is in order. Atony of the bladder wall may be the responsible factor, although it is exceedingly rare; however, great care must be exercised to rule out mechanical obstruction as well as disease of the central nervous system before the final diagnosis of atony is made.

I would like to mention two patients whose obstructions were completely removed, and yet after they left the hospital they had large amounts of residual urine, 750 cc. in one case and 700 cc. in the other. Recent examinations show the complete absence of residual urine in both of these patients.

In a certain number of patients a coexisting pathologic feature is the cause of residual urine, such as one or more large diverticula or a large amount of hydronephrosis. Once in a while a patient may return a year or two after resection with residual urine and a recurrence of the characteristic symptoms. Examination will reveal a carcinoma of the prostatic bed.

HEMORRHAGE

During the early days of resection bleeding during the operation was very troublesome, and instances have been reported in which it became necessary to perform a suprapubic cystostomy in order to control the bleeding. This untoward occurrence led to much discussion. Here again, as in other technical phases of resections, increased experience and persistent search for the bleeding points so that they could be treated with the coagulating current ameliorated matters considerably. Today hemorrhage during the operation has ceased to be much of a problem.

A hemorrhage which occurs during the second postoperative week is probably always due to a secondary infection. Its treatment has become standardized and consists of evacuation of clots, if present, and visualization and fulguration of the bleeding point or points. At times it may be advisable to resect the bleeding area. If the bleeding cannot be controlled, a Foley bag may be used.

Suprapubic cystostomy is rarely if ever needed in this type of case.

In a previous publication I called attention to a type of bleeding that occurs one, two or even three years after resection. I wish to call attention to this type of bleeding because it has not received much consideration in the literature.

When late bleeding occurs one is naturally interested in the cause. It may be due to a stone in the bladder that has formed since the resection, to a tumor of the bladder or to infection in a diverticulum. In some of my cases late bleeding was due to a tumor of the bladder which was resected and fulgurated at the time of the prostatic resection but which had recurred. In an occasional case late bleeding may be due to a renal tumor, nephrolithiasis or hydronephrosis.

In cases of resected carcinoma of the prostate late bleeding is always due to a recurrence of the growth.

If the causes just mentioned have been excluded, careful examination may show the presence of varices in the prostatic urethra and at the internal urethral orifice; however, in the larger number of cases careful examination shows the presence of more or less prostatic tissue, clearly indicating that not enough tissue was removed at the time of the first resection.

Finally, I have never seen late secondary bleeding in cases of small fibrous prostates or median bars.

VASECTOMY

It might be well to call attention to the present trend away from performing vasectomies.

During the early period of resection, vasectomy was recommended and used by a very large number of urologists as a routine procedure, the object of which was to prevent postresection epididymitis.

At the present time there is a decided trend away from vasectomy as a routine procedure.

TABLE 3.—*Amounts of Residual Urine in 234 Recent Patients Tested After Transurethral Resection (Third Series)*

Amount	Cases	
	Number	Per Cent
No residual	210	89.74
11-20 cc.	16	6.83
Total 96.57 per cent		
21-30 cc.	4	1.28
31-40 cc.	1	0.42
41-50 cc.	2	1.28
Over 50 cc.	1	0.42

In my first cases vasectomy was not employed. In 12 per cent of this series there was postresection epididymitis. I then employed vasectomy as a routine for several years.

For the past three or four years I no longer perform vasectomy except under certain circumstances which I shall mention. In my recent experience postresection epididymitis is uncommon. I have reviewed 250 recent cases at random from my records at the Presbyterian Hospital and found that epididymitis developed in only five of them, an incidence of 2 per cent. In rare instances epididymitis may develop two, three or four weeks after the patient has left the hospital, but this complication is exceedingly rare, and if the patient lives outside the city, he may fail to report it. Because of my experience I no longer feel that vasectomy, as a routine procedure, is indicated.

TABLE 4.—*Analysis of Cases with 25 Cc. or More of Residual Urine Following Transurethral Resection*

Patient Age	Residual	Complications	Comment
E. B. 66	25 cc.	Bilateral hydronephrosis, bilateral hydro-ureter	Last check-up 6 months ago
R. E. 69	30 cc.	Urethral stricture, hydronephrosis, hydro-ureter	No urinary difficulty a few weeks ago
C. K. 71	30 cc.	Carcinoma of prostate, bladder diverticulum, prostatic calculi	Under treatment
B. S. 73	30 cc.	Bladder diverticulum, urethral stricture	
J. W. 68	35 cc.	Carcinoma of prostate, bladder diverticulum	Urine clear 6 months ago
J. J. 77	50 cc.	Strictures, prostatic stones, bilateral hydronephrosis, hydro-ureter	No symptoms
C. U. 75	50 cc.	.....	Under treatment
I. W. 68	15 oz.	Hypotonic myogenic bladder	Patient died 7/16/39

Vasectomy is employed for patients who come to the hospital with a severe acute attack of epididymitis and are in need of catheter drainage because of complete retention or a large amount of residual urine and with infected urine. This group is not large.

As has been previously mentioned, the object of the treatment of prostatic obstruction is the complete removal of the obstruction. Whether or not this has been accomplished can best be determined by an examination of the patient for the presence or absence of residual urine.

I wish to present data for three groups of patients who were examined for the presence or absence of residual urine following transurethral resection (tables 1, 2 and 3). Figures for the first two groups have been previously reported.[5] They are presented again for purposes of comparison with the third, or recent, group.

A review of these three groups of patients reveals the interesting fact that there has been a very definite increase in the number who had no residual urine as well as in decrease in the number who had from 10 to 20 cc. In the first group there were 66.3 per cent with no residual, in the second group 75.8 per cent and in the third group 89.7 per cent. Likewise there was a definite decrease in the number who had from 10 to 20 cc., namely, 16.1 per cent, 12 per cent and 6.8 per cent respectively. These two groups made up 82.41 per cent in the first series, 87.9 per cent in the second series and 96.57 per cent in the present series.

Likewise there has been a definite reduction in the number of patients who had over 50 cc. of residual: 7.32 per cent, 3.76 per cent and 0.42 per cent.

In this series there was only one patient who had over 50 cc. of residual urine.

122 South Michigan Avenue.

5. Kretschmer, H. L.: S. Clin. North America **19**: 177-190 (Feb.) 1939.

THE PROPHYLAXIS OF PYELO-URETERITIS GRAVIDARUM

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Pregancy complicated by infections of the upper portions of the urinary tract presents a problem which has baffled obstetricians for many years. Not only have the etiology and course of the disease process not been clearly understood, but its treatment and, more particularly, its prevention have been quite empirical and often lacking in effectiveness. During recent years, intensive work on the problem has clarified some of the factors concerned in the etiology, enabling us to establish means of prevention. In addition, therapeusis of the infection itself has undergone most revolutionary changes, so that now we may view the disease with justifiable equanimity. As some of the more recent modes of treatment are not widely used and because there will always be need for constant vigilance as well as training of physicians to prevent the occurrence of the disease, we present this report, which will outline the treatment in use at the New York Lying-in Hospital as well as give the results of our experience.

Effectiveness in carrying out the provisions of any system of antepartum care designed to reduce morbidity from urinary tract infections requires that some of the etiologic factors be fully appreciated. At the outset, therefore, it may be well to consider those factors that are most essential to our purpose, namely the reduction of the incidence of pyelo-ureteritis.

ETIOLOGY

For an inflammation to develop in the tissues of the kidney pelvis and the abdominal ureter, two conditions must necessarily be existent. The first of these is stasis of urinary flow and the second is the presence of an inflammation-producing agent which can develop in such an environment. Unfortunately for our child-bearing women, in over 80 per cent of them marked stasis develops in the right ureter and, to a lesser degree, in the left one also. We cannot go into all the causes which contribute to the development of this urinary stasis, but for practical purposes it will suffice if we mention two: first, hormonally produced atony of the musculature of the tract and, second, the occlusive effect of the pregnant uterus bearing on the ureters. Atony of the musculature, on the one hand, with the presence of an obstacle to be overcome, on the other, contribute to produce the condition which has come to be recognized as the "physiologic hydro-ureter and hydronephrosis of pregnancy." As stated, this prerequisite to inflammation exists in approximately 80 per cent of pregnant women. Thus pregnancy itself may truly be said to provide the background most suitable for inflammation of the urinary tract, which explains why pyelo-ureteritis is so much more frequently seen during the reproductive period of a woman's life than at any other time, with the possible exception of childhood.

The second prerequisite for infection of the upper urinary tract is an organism capable of living in the environment of the ureter and of producing an inflammatory reaction in the tissues of the ureter and renal pelvis. The pathogenic agent which most frequently qualifies as a primary invader in these respects is some member of the large family of colon bacilli. The secondary invaders are most frequently anaerobic nonhemolytic streptococci, which are relatively nonpathogenic and produce inflammatory effects only in tissues previously injured by some other organism or by trauma. As the human body normally harbors huge numbers of colon organisms, it is not surprising that pregnancy with urinary stasis should be complicated by inflammatory reactions of the urinary tract due to the colon bacillus. How the organisms reach the upper urinary tract is a matter pertinent to our consideration of prophylaxis, so we may well point out that the two most salient factors, in all probability, are constipation of the large bowel and trauma of the lower portions of the urinary tract. Both of these are instrumental in allowing the coliform organisms to reach the upper urinary tract, where, if they arrive in sufficient numbers, they may cause inflammatory effects.

This brief and necessarily incomplete consideration will suffice to explain the causation of primary attacks having their incipience in pregnancy; however, the matter of etiology is unfortunately not quite as simple as this. We must also recognize the fact that previous attacks of pyelo-ureteritis may not have been completely cured and that many women carry a chronic type of afebrile and asymptomatic pyelo-ureteritis for years. This chronic type of infection may flare up as an acute exacerbation when the urinary stasis of pregnancy provides a locus of reduced resistance. An appreciation of the possible role of previous urinary tract inflammation is one of the most necessary points of view for the obstetrician to acquire, if he is to deter the incidence of urinary tract inflammation in the pregnant woman.

INCIDENCE OF PYELO-URETERITIS GRAVIDARUM

The appearance of inflammation of the upper urinary tract complicating pregnancy varies in its frequency and is dependent on many factors which are not wholly understood. For instance, Baird reports an incidence of 15 per cent in the Glasgow Royal Infirmary, whereas van Rooy reports only 0.8 per cent in Amsterdam. A common expectancy would probably vary from 1.5 to 2.5 per cent in communities where women of child-bearing age have average standards of living with adequate nourishment and good medical care.

PATHOLOGIC COMPLICATIONS OF INFLAMMATION OF UPPER URINARY TRACT IN PREGNANCY

Before presenting the means of avoiding the disease, it is well to understand some of the more serious possibilities that we are attempting to obviate. One must consider these in two distinct categories, the immediate and the remote. The immediate hazards which pyelo-ureteritis presents are:

1. Anemia due to the hemolytic effect of the colon organisms on the red blood cells. Although this may not of itself constitute a grave menace, it is often a considerable handicap in treating the disease, which may require blood transfusions.

2. Bilateral involvement of the tracts, which is more serious. Bilateral disease always carries with it a more grave prognosis, which fact will become more evident as we discuss the next possibility.

3. The most serious complication of all, namely ascension of the inflammatory process from the excretory ducts into the

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renal cortex. Whenever this occurs, the obstetrician is confronted by a very serious problem, for not only is the excretion of urine impaired, with the retention of the nitrogenous products of metabolism within the blood stream and tissues of the body, but there is also danger of the patient's dying.

4. The immediate effects of acute pyelo-ureteritis on the fetus, which are of importance also, for premature delivery, stillbirth and even death a few days after delivery are not infrequently seen.

The remote effects on the mother are chiefly due to the fibrosis which the inflammatory reaction induces. This may permanently impair or prevent all peristalsis of the renal pelvis and ureter, resulting in constant hydronephrosis and hydro-ureter of the duct and in reduced secretory activity of the kidney cortex. In addition we must point out that, the longer the acute febrile phase is permitted to exist, the longer will be the period of time necessary to wipe out the infection after the pregnancy is over. Many experiences have impressed us with the truth of this statement, and in addition the literature on urinary tract complications of pregnancy is replete with confirmatory illustrations.

METHODS OF AVOIDING AND MINIMIZING THE DISEASE

With this brief outline of the disease in mind, we may turn to a consideration of the means whereby it may be altered for the benefit of the patient.

The first step which must be taken, and one which cannot be sufficiently stressed, is to obtain the history. Patients must be quizzed by name and symptom to establish or preclude the possibility that previous disease has involved the urinary tract. Over 50 per cent will give no definite history of pyelo-ureteritis at the time the anamnesis is recorded, and then later the patient's mother or aunt will reveal that there was such an event, particularly if an acute exacerbation occurs to remind them of the clinical picture. Emphasis is laid on the importance of the history because the chances that the disease will complicate pregnancy are increased twofold in previous sufferers and therefore one should be particularly observant of this group; but the history is emphasized more especially because the prognosis, should the disease reappear, is more discouraging than that pertaining to the primary acute attack. Not only is the infection more difficult, but in addition the scar tissue in the excretory ducts and the probability of decreased renal function must be taken into account if the best interests of the patient are to be served by her medical advisers.

The history having been taken, the obstetric patients divide themselves into two categories from a urologic point of view: those who have had previous attacks of pyelo-ureteritis and those who have not. First let us consider the antepartum care of the larger group, those who afford no history of previous inflammation of the upper urinary tract.

THE UROLOGIC CARE OF NORMAL OBSTETRIC PATIENTS

At each antepartum visit, the normal obstetric patient should be questioned concerning dysuria, frequency and pain in the kidney region. Should any of these be experienced, a sterile catheter specimen of bladder urine should be obtained and scrutinized microscopically. Should clumped white blood cells be seen, the remainder of the sterile specimen should be sent to the bacteriologic laboratory for culture. In the meantime, fluids are forced and the patient is given 4 Gm. of sodium bicarbonate after each meal. If the culture is positive for Bacillus coli, the patient should be given the ambulatory treatment for urinary tract infection, which will be outlined presently.

Not infrequently the first indication of urinary tract infection is a cloudy precipitate produced in the urine by the test for albuminuria. When this is seen, in the absence of any supportive evidence for the diagnosis of toxemia, a sterile catheterized specimen of bladder urine should be taken and cultured for B. coli, whether any white blood cells are seen in the microscopic specimen or not.

Emphasis is placed on bacilluria as demonstrated by bacteriologic culture of the urine. This should be the basis of prophylaxis and not symptoms or the presence of pus cells in the urine.

As soon as the positive report of bacteriologic culture for B. coli is obtained, the patient is placed on what we have named our ambulatory sulfanilamide treatment. The patient is provided with twenty-five 5 grain (0.3 Gm.) tablets of sulfanilamide and is instructed to take one tablet on awakening, one after each meal and a fifth on retiring. With each of the postprandial pills the patient is instructed to take a teaspoonful of sodium bicarbonate dissolved in water. Fluids are limited to the lowest amount consistent with comfort (about 1,500 cc. daily). Of all the patients treated in this way, numbering about 200, only two have shown idiosyncrasy to the drug. With these small doses, the concentration of sulfanilamide in the blood rarely goes above 2 mg. per hundred cubic centimeters. Not only would this concentration seem devoid of danger, but many will wonder that it can be efficacious in a curative way. We shall offer statistics which prove beyond a doubt that the treatment is valuable in controlling the early stages of the infection.

The patient then returns for a repeat urine culture in a week's time. Even though the culture is negative, the course just described is repeated after one week's rest until a series of three negative urine cultures are obtained. Thereafter the urine is cultured once a month until delivery. Should a positive culture again be obtained, the ambulatory sulfanilamide therapy is repeated.

In brief, this constitutes the treatment of incipient cases. However if, as occasionally happens, the ambulatory treatment does not prove effective so that symptoms of pyelo-ureteritis such as pain in the costovertebral angle or persistence of pyuria occur, the patient is examined by cystoscope, the ureters are catheterized and bilateral ureteral cultures and pyelograms are taken. In this way the presence of inflammatory strictures of the ureter, hydronephrosis and hydro-ureter greater than those which occur physiologically are recognized, and appropriate treatment is instituted.

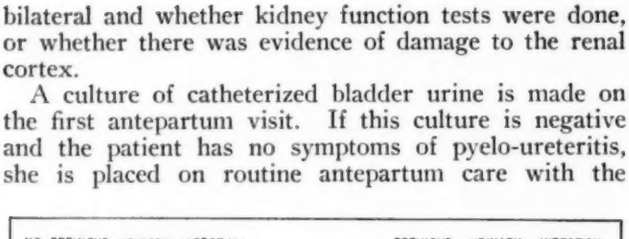
UROLOGIC CARE OF OBSTETRIC PATIENTS WHO HAVE HAD PREVIOUS INFECTIONS OF THE UPPER URINARY TRACT

The patient who offers a history of previous infection of the urinary tract is treated quite differently in that she is given less leeway because of the greatly increased chance of the development of infection during pregnancy.

If possible, contact is made with the hospital or physician who treated the previous infection, with a view to obtaining data concerning its severity and duration as well as whether the process was unilateral or

bilateral and whether kidney function tests were done, or whether there was evidence of damage to the renal cortex.

A culture of catheterized bladder urine is made on the first antepartum visit. If this culture is negative and the patient has no symptoms of pyelo-ureteritis, she is placed on routine antepartum care with the


NO PREVIOUS URINARY INFECTION
1. OBSERVATION FOR SYMPTOMS
2. WITH ONSET OF SYMPTOMS CATHETERIZED URINE MICROSCOPIC - SEDIMENT
3. IF CLUMPED W. B. C. FOUND CULTURE SODIUM BICARBONATE FORCE FLUIDS
4. IF CULTURE POSITIVE FOR B. COLI
5. CULTURES REPEATED
6. IF CULTURE REMAINS POSITIVE CYSTOSCOPY URETERAL CULTURES KIDNEY FUNCTION PYELOGRAMS SULFANILAMIDE REPEATED
AMBULATORY SULFANILAMIDE TREATMENT
1. SULFANILAMIDE 0.3 GM. 5x DAY FOR 5 DAYS
2. SODIUM BICARBONATE
3. LIMIT FLUIDS
4. REPEAT AFTER ONE WEEK
PREVIOUS URINARY INFECTION
1. ABSTRACT OBTAINED FROM PHYSICIAN OR HOSPITAL
2. URINE CULTURE TAKEN ON FIRST VISIT
3. CULTURE POSITIVE
CULTURE NEGATIVE
CYSTOSCOPY URETERAL CULTURES
KIDNEY FUNCTION PYELOGRAMS
SULFANILAMIDE TREATMENT
MONTHLY CULTURE
CULTURE DURING PUERPERIUM
TWO CULTURES AFTER DISCHARGE
4. CULTURES REPEATED
5. PATIENT SEEN BIWEEKLY

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addition that urine cultures are repeated at monthly intervals until term; one is made in the puerperium and two after discharge from the hospital.

If, on the other hand, the initial urine culture is reported as positive for B. coli or anaerobic nonhemolytic streptococci, this together with the history of previous infection establishes the diagnosis of chronic inactive urinary tract infection and places the patient in a group which will receive very special attention and consideration, for in our experience over 40 per cent of them will develop an acute exacerbation before pregnancy has reached term if they are not given preventive care. A majority of these patients are examined by cystoscope and given bilateral renal function tests, while pyelograms are usually made at the same visit to determine gross abnormalities in the tract. Such a

TABLE 1.—*Treatment of Acute Attack of Pyelo-Ureteritis*

1. Hospitalization
2. Complete bed rest
3. Microscopic examination of urine
4. Bladder culture
5. Blood chemistry every two days
6. Intravenous pyelograms
7. Large doses of sulfanilamide

TABLE 2.—*Treatment of Patient in Puerperium*

1. Careful follow-up until three successive negative cultures are obtained at intervals of one month
2. Contraception for two years
3. Cystoscopy to rule out strictures
4. Repeated courses of sulfanilamide

patient is given the ambulatory sulfanilamide treatment in addition. If the tract shows no serious abnormality except the positive urine culture, she is followed at bi-weekly intervals to observe evidences of the early stages of the acute phase. In addition she is warned that, if kidney pain should supervene or if there should be chills and fever, she is to come to the hospital at once. On the other hand, if such an eventuality does not occur, it is entirely possible that the ordinary antepartum antipyelitis regimen of forced fluids, frequent rest in the horizontal position during the day, with careful attention to adequate bowel elimination, and a broad general diet may suffice to carry the cooperative patient through to term, delivery and the puerperium without an acute attack. The postpartum care of all patients as a single group will be treated presently.

THE ACUTE ATTACK

Whether the acute attack occurs as a primary entity or as a recrudescence of long-standing disease, certain elements of therapy are fundamental. The first is hospitalization. Here bed rest in the completely recumbent position or with the foot of the bed elevated is given. Bladder cultures are repeated together with microscopic examination of the urine, to determine the type and severity of the inflammatory reaction. The blood nonprotein nitrogen level is determined every second or third day to rule out nitrogenous retention due to cortical damage. Intravenous pyelograms are taken to throw the kidney pelves and ureters into view and also to give information as to kidney function. In addition, these patients are given large doses of sulfanilamide commencing with from 6 to 8 Gm. a day in divided dosages, with limited fluid intake the first two days, and thereafter a dose of the drug sufficient to maintain a concentration in the blood of from 8 to 10 mg. per hundred cubic centimeters and concentration in urine above 100 mg. per hundred cubic centimeters. With the great majority of patients the temperature returns to normal after a few days of this treatment, and after three or four days of normal temperature the patient is discharged to be followed in the antepartum clinic.

TABLE 3.—*Results of Prophylactic Routine*

	Before Sept. 1937	After Sept. 1937
Incidence of suspected cases of pyelo-ureteritis	2.02%	1.06%
Incidence of proved cases of pyelo-ureteritis	0.80%	0.47%
Average duration of febrile phase	10.4 days	5.4 days
Average time after onset to obtain negative cultures	135 days	50 days
Negative cultures obtained during pregnancy	0	55%

Much to our surprise, about 25 per cent of the patients undergoing a primary acute attack who are admitted early in the febrile phase not only undergo remission but are also cured of their bacilluria. This is a distinct advance over older forms of therapy, experience with which yielded a widely accepted dictum to the effect that no patient was ever rendered bacteria free during pregnancy.

If, on the other hand, both ureters are involved and if the patient stores nitrogen as the result of persistent renal damage, interruption of the pregnancy has to be considered, just as in the older forms of treatment. However, in our experience, if there is careful observation so that the acute phase comes to treatment early and particularly if the acute phase is treated vigorously from the first, these more serious eventualities will seldom be met. In the past eighteen months we have been forced to induce labor prematurely on only one occasion, in marked contrast to our earlier experience.

TREATMENT OF THE PATIENT IN THE PUERPERIUM

The criterion of cure is three successive negative urine cultures taken at intervals of one month. This routine demands careful follow-up of the patient. In

addition, further pregnancy is interdicted for a period of two years and the patient is given contraceptive advice and instruction in a technic suited to her needs.

Patients who have persistently positive urine cultures are given cystoscopic examination, and the possibility of ureteral strictures is ruled out. In addition, they are given repeated courses of sulfanilamide treatment until the desired negative urine cultures are obtained. In our experience, the longer the acute phase has existed the more difficult these final procedures become. We have had a few patients who have resisted all attempts to sterilize the urine for many months, and one for three years, which indicates clearly the importance of early recognition of the prodromal symptoms and prompt alleviation of the early forms of the acute attack.

RESULTS OF THE PROPHYLACTIC ROUTINE

Before September 1937, at which time this plan of care was instituted, the incidence of pyelo-ureteritis complicating pregnancy was 2.02 per cent including those having a majority of the symptoms of the disease and 0.80 per cent including only those who presented the well developed syndrome satisfying all criteria. Since September 1937 the incidence in the two groups has dropped to 1.06 per cent for clinically suspected cases and 0.47 per cent in the unquestionable group. In other words, the incidence of the disease has been reduced 50 per cent.

Just as important as the reduction of the incidence is a similar reduction in the duration of the febrile phase from 10.4 days, which was the average formerly, to 5.4 days, which is the record during the past eighteen months. This has a dual significance in that the briefer the febrile phase, the sooner the patient may be rendered bacteria free, thereby effecting an economic saving and enhancing the welfare of the patient.

Formerly it required an average of 135 days from the date of the acute attack to secure bacteria-free urine; now the average is fifty days after the onset of the disease.

As stated before, we now are able occasionally to sterilize the urine during pregnancy, that is, in about 55 per cent of cases, whereas formerly this was almost never possible. However, there are always a few patients who are disappointing, and our experience is no exception. We have two patients who have been treated most carefully and who have had repeated courses of sulfanilamide as well as cystoscopic treatment and who, despite our best efforts, continue to put out large numbers of coliform bacilli in the urine after many months of treatment.

Postpartum pyelitis has been almost completely eliminated by the use of small doses of sulfanilamide and sodium bicarbonate administered prophylactically to all patients having infected bladder urine with symptomatic cystitis.

In addition, pyelonephritis has come to be almost nonexistent because we do not allow the disease to progress to the point where this complication is possible.

SUMMARY

1. An antepartum routine designed to detect the earliest stages of upper urinary tract infection has been successful in pointing out patients who have primary attacks as compared with those having repeated exacerbations.

2. In the former group, small doses of sulfanilamide given with sodium bicarbonate have been useful in obviating the disease in the prodromal phases. The incidence of febrile disease has been reduced 50 per cent.

3. Early availability of hospital care with vigorous treatment has succeeded in reducing the febrile phase by 66 per cent, as well as the length of stay in the hospital and the length of time necessary to render the urine sterile in the puerperium.

4. The more severe complications of the disease in the mother and child seem to have been largely obviated.

A BASIC UNDERSTANDING OF VARICOSE VEINS

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This article is being presented primarily for the benefit of the general practitioner in an attempt to clarify any confusion that may exist concerning the tests used in the examination of patients who have varicose veins. Any one who has perused the recent literature concerning varicose veins will verify the statement that the varied labeling of the classic Trendelenburg test is confusing and frequently contradictory. In one of the most widely read surgical publications, articles of two well known writers in this field appeared a year apart in which were stated absolutely opposite meanings of a "negative Trendelenburg." The simple test has been expanded to include such modifications as "positive," "double positive," "negative" and "nil." Add to this, as examples, Perthes' test, the tight bandage test, the comparative tourniquet tests and the Schwartz test. Is confusion not to be expected from such a situation? The practicing physician desires only to know what is wrong and how to correct it. So we will purposely not elaborate on or attempt to reexplain these obviously confusing nomenclatures. Literature has amplified them to the extreme. Our interest is to find out what is wrong anatomically and physiologically. That and the classification of observations under respective headings are primary. Rational therapeutics will then follow as a matter of course.

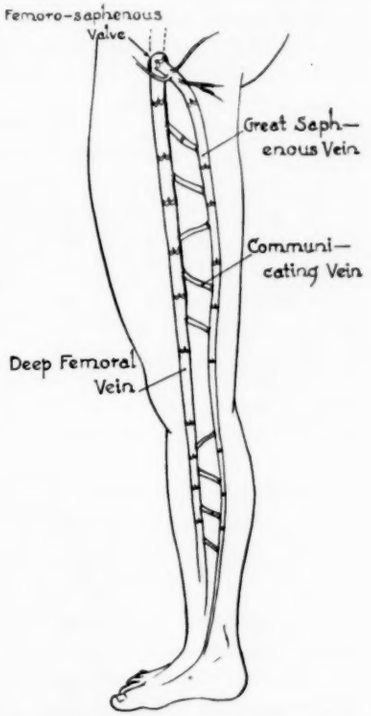


Fig. 1.—A simple diagrammatic scheme of the venous return from the lower extremity. The lesser saphenous vein has purposely been omitted.

From the Section on Postoperative Care (Dr. Heyerdale), the Mayo Clinic.

The pathologic physiology of an incompetent saphenous vein was described by Trendelenburg [1] in 1890. He graphically demonstrated the reversal of blood flow and attributed this condition to disruption of valves at the saphenofemoral junction. On this basis he devised the simple yet adequate test for a definitely incompetent

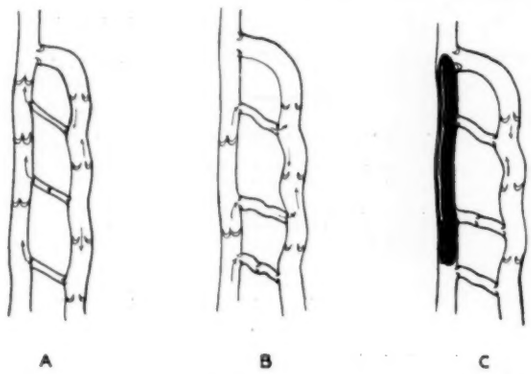


Fig. 2.—Incompetence of the three anatomic systems: *A*, inadequate superficial saphenous system; *B*, an incompetent communicating system (associated with failure of the superficial saphenous system); *C*, obstructing thrombosis of the deep system; compensatory dilatation of the superficial veins is necessary for adequate venous return.

greater saphenous system, a test which today bears his name. Yet forty-four years before Trendelenburg's paper Sir Benjamin Brodie [2] had described exactly the same method for determining the status of the superficial venous return from the legs. So we are detracting nothing from the credit of Trendelenburg when we urge physicians to discard the practice of employing a man's name to designate these tests and to speak rather in terms of what these tests indicate. In that way we shall train ourselves to visualize more perfectly the significance of each test, what is wrong and what is the rational method of treatment.

Venous return from a lower extremity is accomplished through two superficial saphenous systems and through a deep system. The superficial and deep routes are connected with one another by numerous communicating veins. These channels are necessarily equipped with valves to aid in the ascent of the venous blood and to prevent retrograde flow. Probably the most important valve is situated at or in close proximity to the saphenofemoral junction. Its impairment leads to gross incompetence of the greater saphenous vein. These are the simple relevant facts of normal anatomy and are represented in diagrammatic form in figure 1.

When visible and palpable varicosities are present there are three venous systems, anatomically, which may be affected: the superficial, the communicating and the deep (fig. 2).

INCOMPETENT GREATER SAPHENOUS (SUPERFICIAL) SYSTEM

The greater saphenous system should be the first to be investigated. The patient stands upright before the examiner with both legs fully exposed from the groin downward. The degree of dilatation and the distribution of the tortuous veins, the presence or absence of edema and cutaneous changes are noted. Palpation is of more value than inspection, for often large tortuous veins, not noticeable to the eye, can be felt in the subcutaneous tissues. To demonstrate incompetence of the venous system, the following method is probably the most practical: The fingers of one hand are placed over the great saphenous vein, usually at the fossa ovalis, while the fingers of the other hand percuss a dilated segment of vein in the leg below. The percussion stroke is an abrupt thrusting one so as to give rise to an impulse, much after the manner in which free fluid in an abdomen is detected by means of percussion. If the fingers at the fossa pick up a definite and strong impulse, incompetent valves and a dilated main saphenous trunk are strongly to be suspected. Proof, however, is established by a reversal of the procedure. If percussion of the vein at the fossa or in the upper portion of the thigh produces an impulse which travels downward to the fingers below, and can be definitely felt, we know that the valves are incompetent and that the vein does not, and never will, perform its normal function. For such an impulse cannot travel distally in the vein if the valves are competent (fig. 3).

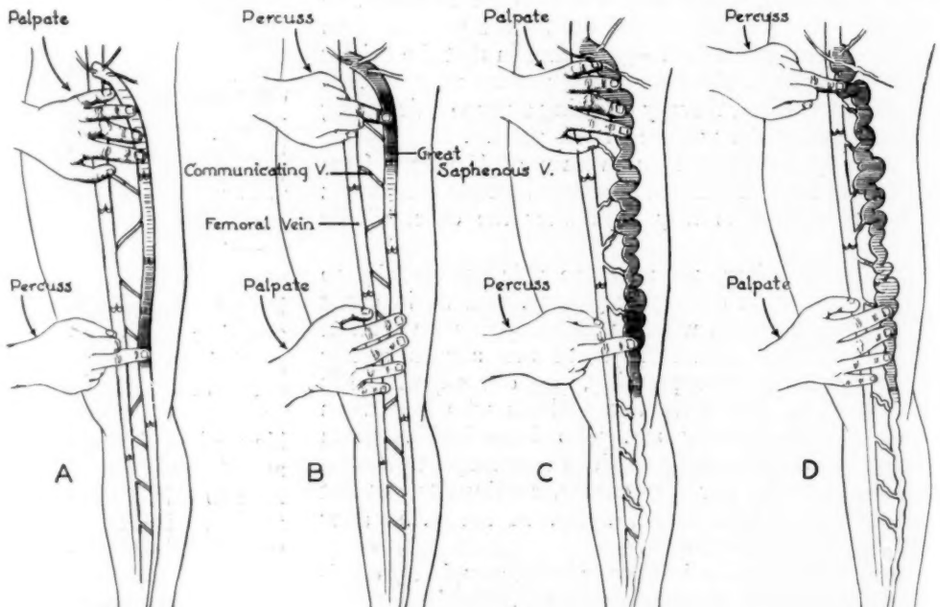


Fig. 3.—Testing for an incompetent greater saphenous system: *A* and *B*, a normal competent vein; intact valves prevent downward passage of the impulse; *C* and *D*, procedure used in detecting incompetent veins in which the valves do not impede the free passage of a strong impulse in both directions.

Owing to mechanical difficulties, such as marked obesity of the patient or extreme tortuosity of the

1. Trendelenburg, Friedrich: Ueber die Unterbindung der Vena saphena magna bei Unterschenkelvaricen, Beitr. z. klin. Chir. **7**: 195-210 (Nov.) 1890.

2. Brodie, B. C.: Lectures Illustrative of Various Subjects in Pathology and Surgery, London, Longman (and others), 1846, vol. 7, pp. 157-191.

varices, only faint descending impulses may be discerned in some instances. The type of treatment then depends on the judgment of the examiner and his estimate of the amount of varicosities and the degree of vascular stasis present.

Examination of the superficial veins is never complete without a thorough investigation of the lesser saphenous system, which drains the posterior and lateral aspects of the leg. Pathologic changes in the lesser saphenous system may be identical with those found in the greater saphenous system and the diagnosis can be made in the same manner. Treatment also is comparable and will be outlined. Various segments of the varicose trunks can be explored in like manner, and whenever we find a strong, definite, distalward impulse, we know that no adequate valve intervenes.

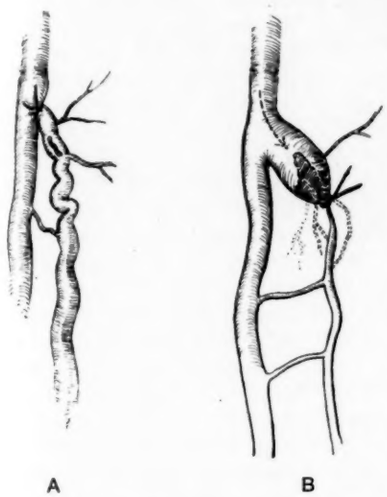


Fig. 4.—Ligation: *A*, correct site of ligation at the saphenofemoral junction; *B*, incorrect ligation, which leaves a blind stump to encourage the formation of new varicosities and to provide a site for the formation of a free thrombus (a ready source for multiple pulmonary emboli).

Although it is not necessary, we can confirm our deductions on the definitely incompetent greater saphenous veins by use of a tourniquet applied on the highest accessible portion of the thigh with the leg elevated and the veins drained of their blood. If, on standing, the veins fill rapidly from above downward after release of the tourniquet, we know that the valves do not hold; the vein is incompetent. In a similar way the lesser saphenous vein can be tested with a tourniquet applied just below the level of the popliteal space.

In conclusion, one should record whether the superficial saphenous systems are competent or incompetent and not that a certain test is "positive" or "negative." One can qualify the statement, if one wishes, by stating "as tested by palpation and percussion of the veins or by using a tourniquet." Use of the words "positive" and "negative" is likely to cause confusion when applied to any test, first because these terms are ambiguous and second because, if such terms are applicable at all, it is the result of a test and not the test itself that has "positive" or "negative" significance.

Brief mention should be made of the rational therapy for incompetence of the superficial saphenous systems pertinent to the pathology and physiology involved. Downward pressure of the column of blood in the inferior vena cava, common iliac, femoral and greater saphenous veins, unsupported by adequate valves, encourages further dilatation and elongation of the already varicose distal segments and provokes the gradual development of varices in previously unaffected veins. Local injections of sclerosing fluids alone for the obliteration of visible varices are likely to be followed by recurrences, particularly if the region treated is subjected to direct pressure from above. Such treatment is like clipping off the tops of weeds in the hope that they will not grow again. The roots must be destroyed in order to obtain such a result. So it is with the reversed flow of blood in the incompetent greater saphenous system. It must be interrupted first at the saphenofemoral junction and then obliterated from that point distalward.

Cumulative experience has stressed the importance of high ligation of the incompetent greater saphenous vein in the prevention of recurrences. The ligation should be made at the fossa ovalis, exactly at the junction of the saphenous and femoral veins, without leaving any stump to encourage the formation of future varicose channels or to allow a free thrombus to form. Division of the vein between the two sites of ligation should be performed and a segment of vein should be excised at this site. All tributary veins joining the saphenous vein in this region also should be ligated and severed. This definitely lessens the probability of future recanalization (fig. 4).

Following ligation, retrograde injection of a sclerosing fluid (from 2 to 4 cc. of 5 per cent sodium morrhuate solution), as indicated, into the distal segment of vein is recommended as a valuable adjunct. The patient is allowed to be ambulatory immediately after operation and is not hospitalized further. Subsequent obliteration of the remaining varicosities is accomplished by repeated injections usually from above downward. If adequate ligation is not performed on an incompetent greater saphenous vein, recurrences are to be predicted. Of course, there are many cases of mild or moderate varicosities in which the saphenous systems are not incompetent. In such cases injection therapy alone suffices.

INCOMPETENT COMMUNICATING VEINS

Incompetent communicating veins are relatively uncommon, although much has been written concerning them. They are almost always associated with an incompetent greater saphenous vein, and clinical detection is easy. After the leg is elevated in order to allow the veins to be drained of their blood by gravity, a tourniquet is placed high on the thigh. The patient is then allowed to stand upright with the tourniquet still applied; if the varicosities fill rapidly within thirty seconds, it is assumed that there has been an overflow from the deep to the superficial circulation. In other words, the valves of the communicating vein or veins are incompetent. To eliminate error one must apply the tourniquet only tightly enough to obstruct the superficial veins (fig. 5).

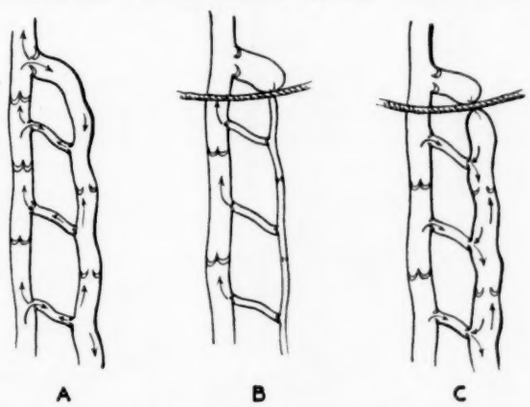


Fig. 5.—*A*, incompetent superficial and communicating systems; *B*, competent communicating system with tourniquet preventing reversal of flow in the incompetent superficial system; *C*, incompetent, communicating and superficial systems; an overflow from the deep to the superficial circulation through incompetent communicating veins with rapid dilatation of the superficial veins when the leg is lowered.

Again for the sake of emphasis, let us stress the importance of stating the status of a system in terms

of competence or incompetence, thereby avoiding the expression "positive test" or "negative test."

Since incompetent communicating veins are usually associated with incompetence of the greater saphenous system, and since treatment for incompetent communicating veins involves, first, treatment for incompetence of the greater saphenous system, detection of the presence of incompetent communicating veins is not particularly vital. We believe that the injection of sclerosing fluids into the distal segment at the time of high ligation and subsequent injection of such fluids into the remaining varices will prevent retrograde flow through the communicating veins. This method, too, might be a subject for discussion and may have its uncertainties and occasional failures, but from a practical and financial standpoint it is preferable to extensive operative ligation of each communicating stem. If a recurrence follows at the site of the incompetent communicating vein, one may limit the segment of vein affected by the sclerosing fluid by injecting the vein between two tourniquets. The results are usually excellent with the formation of a firm thrombus in the offending segment adjacent to the incompetent communicating vein.

INCOMPETENT DEEP VENOUS SYSTEM

Persistent occlusion of the deep veins is a comparatively rare phenomenon, but it does occur. It is usually associated with marked edema and cutaneous changes. If edema is absent, one can almost exclude per se the possibility of complete blockage in the deep venous system. Usually there is a definite history of phlebitis with fever, soreness and swelling of the leg. Therefore, if it is suspected that such a condition exists, it is inexcusable for a physician not to determine its presence by applying a conclusive and simple test (fig. 6). A Para gum rubber bandage is applied around the leg usually from the instep to just below the knee or as far up the thigh as indicated. The patient is then instructed to walk about with this in place and to note whether with this activity his discomfort is increased or diminished. If the flow through the superficial venous system is a compensatory one, the constriction caused by the bandage will result in acute severe discomfort, because those veins which have assumed the function of allowing a return flow of blood from the extremity are compressed. Usually the patient returns within ten minutes with the bandage in his hand and with an indignant expression on his face. Whereas, if the flow in the superficial veins is not compensatory and if a block is not present in the deep circulation, the bandage usually will give relief by collapsing the useless superficial varicosities.

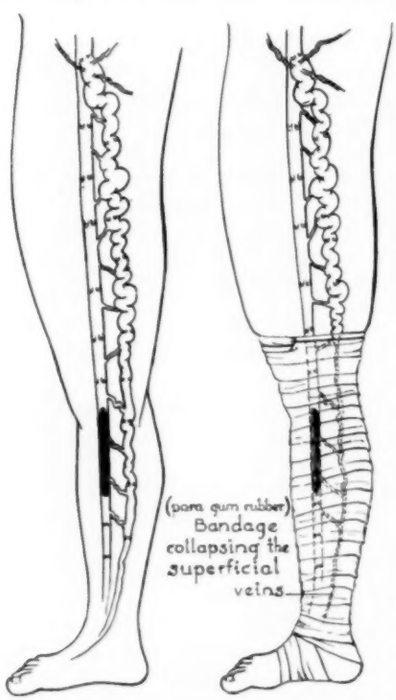


Fig. 6.—The only conclusive test for demonstrating an obstruction in the deep venous circulation. When such a condition is present, severe pain soon results from the blockage of venous return.

The Perthes test is used in a routine manner by many to determine the status of the deep venous circulation. In the majority of instances it probably gives the information desired, and yet many do not realize that there is an inherent flaw in the test. If a segment of a deep vein is obstructed by a thrombus anywhere below the upper level of the tourniquet, it is anatomically possible for a portion of the superficial circulation to detour around the thrombosed deeper vein and return to this vein proximal to the obstructed site. The tourniquet occludes the superficial veins only at one point high in the thigh and will therefore not obstruct this lower portion, which serves in the shunting mechanism. As this may easily occur, an incorrect interpretation results. The physician may then block unknowingly with sclerosing fluids the superficial detour, and venous return from the lower extremity will be hindered even more than it was prior to such treatment. Therefore the test is inadequate, for this one flaw makes it unreliable (fig. 7). The bandage test is by far the better, for it definitely answers the question of whether the deep veins are patent or occluded. Obliterative therapy of any type, when definite deep venous occlusion is present, is absolutely contraindicated. Rest, elevation of the affected extremity, the application of heat and proper external support are the measures to be relied on.

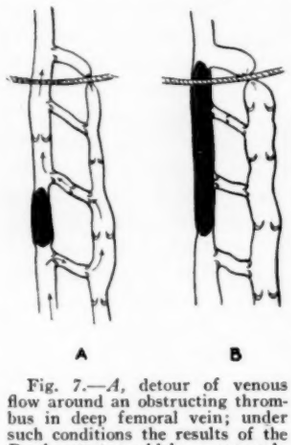


Fig. 7.—*A*, detour of venous flow around an obstructing thrombus in deep femoral vein; under such conditions the results of the Perthes test would be erroneously interpreted as normal; *B*, thrombus in deep circulation extends up to site of tourniquet; it is only in such a condition that the Perthes test can be correctly interpreted.

SUMMARY

Acquaintance with the simple anatomy and physiology of the venous system of the lower extremities tends to clarify the confusion which exists with regard to test procedures and types of treatment for varicose veins. We urge abandonment of specific names for the various tests and acceptance of universal terms based anatomically on the three venous systems to be treated; that is, a test for competence or incompetence of the superficial saphenous system, a test for competence or incompetence of the communicating veins and a test for patency or occlusion of the deep venous system.

Renal Glycosuria.—In a small proportion of subjects glycosuria is due to apparently abnormal renal permeability. There are no precise figures concerning the incidence of this disorder, but it probably occurs about once out of every 300 to 500 cases of glycosuria. Renal glycosuria is a benign condition and is related to a low renal threshold. It is therefore distinguished from diabetes mellitus by the fact that the glycosuria is not accompanied by hyperglycemia; indeed the opposite condition of hypoglycemia may prevail.—Bodansky, Meyer, and Bodansky, Oscar: Biochemistry of Disease, New York, Macmillan Company, 1940.

THE DISTURBANCE OF CARBOHYDRATE METABOLISM IN HYPERTHYROIDISM

NATURE AND MANAGEMENT

T. L. ALTHAUSEN, M.D.

SAN FRANCISCO

A significant and in some instances severe disturbance of carbohydrate metabolism has long been recognized in many patients with hyperthyroidism. Glycosuria, postprandial hyperglycemia and impaired dextrose tolerance occur in these patients and suggest the presence of diabetes mellitus. According to published data, the incidence of the first two factors varies greatly. However, the more or less uniform results of the dextrose tolerance test obtained by different investigators show that reduced tolerance to sugar is found in about one half of the patients with hyperthyroidism. A low respiratory quotient in the fasting state and a tendency to acidosis increase the resemblance of these symptoms of hyperthyroidism to diabetes. Finally, the aggravation of diabetes when hyperthyroidism is superimposed on it also points in this direction.

On the other hand, according to several metabolic criteria, the capacity of the tissues to utilize sugar is reduced in diabetes, while in hyperthyroidism it is increased. After the administration of dextrose in diabetes, the arteriovenous blood sugar difference is less than normal. This observation indicates that less sugar is taken up by the muscles. After a carbohydrate meal, the rise in the respiratory quotient is insignificant. When the supply of carbohydrates in the body is increased, the fall in the organic phosphates of the blood is less than normal. This fall is caused by the formation of a hexose-phosphate compound in the process of utilization of dextrose by the tissues. In contrast, after administration of dextrose in hyperthyroidism a normal or increased arteriovenous blood sugar difference is found [1] in spite of an increased rate of blood flow. After a carbohydrate meal the rise in the respiratory quotient is higher and the fall is more rapid than normal.[2] The fall in the inorganic phosphates of the blood is normal.[3] Finally, Mirsky and Broh-Kahn [4] recently obtained direct evidence from experiments on eviscerated rabbits that in hyperthyroidism the utilization of dextrose by the tissues is notably increased.

Opinions differ concerning the nature of the disturbance of carbohydrate metabolism in the hyperthyroid state. Aside from general statements that "toxic" or "nervous" influences are at work, several specific hypotheses have been advanced. Some writers attribute the disturbance to dysfunction of the pancreas or to inhibition of the peripheral action of insulin. Others hold responsible the abnormal mobilization of hepatic glycogen which is caused by stimulation of the adrenals,[5] or a primary increase in hepatic glycogenolysis.[6] Still others offer as explanation the inability of the liver to store glycogen because of the toxic effects of thyroxine,[2] or increased oxidation of carbohydrates in the tissues which leads to a secondary exhaustion of glycogen reserves.[7] However, none of these hypotheses explain all the abnormal manifestations associated with the metabolism of carbohydrates in hyperthyroidism.

The point of view of the "diabetic" school, which had among its many adherents Naunyn,[8] Falta,[9] von Noorden [10] and Murray,[11] deserves special attention because it has exerted and still is exerting by far the greatest influence on therapy of disturbed carbohydrate metabolism in hyperthyroidism. In recent years this point of view has been championed by Shpiner,[12] who on the basis of his experiments with animals postulated the possibility of a toxic effect of thyroxine on the islet tissue of the pancreas. Hirschberger [13] came to the same conclusion from his studies on the dextrose tolerance of patients with hyperthyroidism following the administration of two successive doses of dextrose according to the method of Staub. The prevalent clinical point of view was given by John [14] in the following statement:

> I think that the explanation of the disturbed carbohydrate metabolism associated with hyperthyroidism is not found in the state of hyperthyroidism per se, but that it is due rather to some other factor which I believe is a "diabetic anlage" that was present in the patient before the hyperthyroidism developed . . .

Intestinal Absorption of Carbohydrates in Normal, Hyperthyroid and Thyroidectomized Rats

Experimental Condition	Substance Administered	Amount Absorbed in 1 Hour per 100 Gm. of Weight, Mg.
Normal	Dextrose	171 ± 14*
Hyperthyroid	Dextrose	284 ± 30
Thyroidectomized	Dextrose	91 ± 5
Normal	Galactose	187 ± 27
Hyperthyroid	Galactose	273 ± 18
Normal	Starch	126 ± 24
Hyperthyroid	Starch	196 ± 14

* Standard deviation.

The incidence of diabetes in hyperthyroidism is 2.1 per cent. The incidence of diabetes at large is given as 1 per cent. There is thus a 100 per cent increase of diabetes in cases of hyperthyroidism. I am inclined to think that a big factor here is the question of overeating which is automatically brought about by the increased metabolism. . . . This throws a great load on the insulogenic apparatus.

John added that the "nervous regulatory mechanism" and hyperadrenalism may exert some influence.

Aided by a grant from the Christine Breon Fund for Medical Research.

From the Department of Medicine, University of California Medical School.

Read before the annual meeting of the Association for the Study of Goiter, Cincinnati, May 22, 1939.

1. Trumper, Max, and Cantarow, Abraham: Biochemistry in Internal Medicine, Philadelphia, W. B. Saunders Company, 1932, p. 45.

2. Sanger, B. J., and Hun, E. G.: The Glucose Mobilization Rate in Hyperthyroidism, Arch. Int. Med. **30:** 397 (Sept.) 1922.

3. Katayama, I.: Significance of Changes in the Composition of the Blood and Urine After Ingestion of Glucose, J. Lab. & Clin. Med. **11:** 1024 (Aug.) 1926.

4. Mirsky, I. A., and Broh-Kahn, R. H.: The Effect of Experimental Hyperthyroidism on Carbohydrate Metabolism, Am. J. Physiol. **117:** 6 (Sept.) 1936.

5. Cramer, William: On the Thyroid-Adrenal Apparatus and Its Function in the Heat Regulation of the Body, J. Physiol. **50:** XXXVIII, 1916.

6. Richardson, H. B.; Levine, S. Z., and Du Bois, E. F.: Clinical Calorimetry: XLI. The Storage of Glycogen in Exophthalmic Goiter, J. Biol. Chem. **67:** 737 (March) 1926. Charvát and Gjurič: The Question of Liver and Tissue Glyco-Regulation, Rozpr. II třídy české Akad., 1926, No. 26, p. 36; cited by John.[14]

7. Johnston, J. A.: Carbohydrate Metabolism: II. Rôle of the Thyroid Gland, Am. J. Dis. Child. **48:** 1015 (Nov.) 1934. Charvát and Gjurič.[6]

8. Naunyn, Bernhard: Der Diabetes mellitus, ed. 2, Vienna, A. Hölder, 1906, p. 99.

9. Falta, Wilhelm: Ueber Glykosurie und Fettstühle bei Morbus Basedowii: Zugleich ein Beitrag zur Röntgentherapie dieser Krankheit, Ztschr. f. klin. Med. **71:** 1, 1910.

10. von Noorden, C. H.: Zuckerkrankheit und ihre Behandlung, Berlin, A. Hirschwald, 1912, p. 50.

11. Murray, G. R.: The Relationship Between Graves' Disease and Diabetes, Clin. J. **34:** 244, 1909.

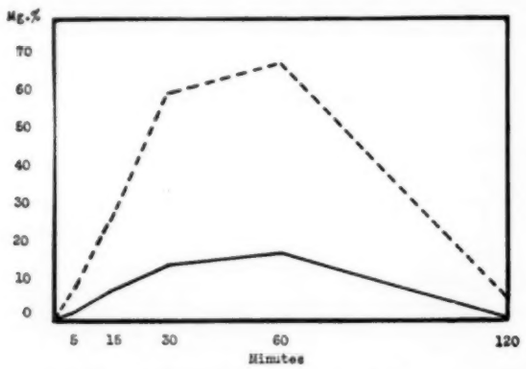
12. Shpiner, L. B.: Increased Metabolism Only One Factor in the Production and Maintenance of the Hyperglycemia and Glycosuria in Experimental Hyperthyroidism, Am. J. Physiol. **92:** 672 (April) 1930.

13. Hirschberger, Cilly: Zuckerbelastungen bei Hyperthyreosen nach dem Prinzip von Staub und Traugott, München. med. Wchnschr. **80:** 804 (May 26) 1933.

14. John, H. J.: Hyperthyroidism Showing Carbohydrate Metabolism Disturbance, J. A. M. A. **99:** 620 (Aug. 20) 1932.

On the basis of this hypothesis many patients with hyperthyroidism who also have glycosuria, hyperglycemia after meals or high dextrose tolerance curves are subjected either to dietary limitation of carbohydrates or to treatment with insulin, or to both, especially if they show a tendency to acidosis.

Approaching this problem through animal experimentation, my associates and I have shown by direct studies of intestinal absorption in rats that administration of thyroxine has a pronouncedly accelerating influence on the intestinal absorption of utilizable sugars and of starch, as shown in the table. Conversely, thyroidectomy causes marked slowing of the absorption of dextrose from the intestine. A series of experiments reported elsewhere [15] gives evidence that the thyroid hormone influences intestinal absorption chiefly through stimulation of phosphorylation. In phosphorylation a given substance is esterified with phosphoric acid. Phosphorylation takes place in the intestinal mucosa. Through constant transformation of a diffusing substance (for example the transformation of dextrose into hexose-phosphate) the gradient for diffusion of a given substance into the mucosa is kept high and its rate of absorption from the lumen of the intestine is thereby increased. The following conditions were ruled out as factors accelerating intestinal absorption in experimental hyperthyroidism: depletion of carbohydrates, increase in basal metabolism per se, rise in the velocity of the blood flow, intestinal hyperperistalsis, and increased permeability of the intestinal mucosa.



Average galactose tolerance curves of ninety-seven persons without thyroid disease (solid line) and 130 patients with hyperthyroidism (broken line).

The accelerating influence of the thyroid hormone on intestinal absorption of sugars was observed in clinical hyperthyroidism. A standard amount of galactose was administered to each of 130 patients with this disease, and the galactose curve of the blood [16] was followed in each case. With one exception all these patients had high curves for galactose in the blood. The average galactose curve in hyperthyroidism was more than three times as high as the average curve for this sugar in ten normal volunteers or in eighty-seven patients with diseases other than hyperthyroidism, as shown in the chart. In order to rule out the possibility that the high oral galactose tolerance curves were caused by impaired utilization of galactose, this sugar was administered intravenously and the rate at which it disappeared from the blood stream was determined in patients with hyperthyroidism as compared with normal individuals.

The stimulating effect of the thyroid hormone on absorption of sugar in human beings was confirmed by the observations that the galactose curve returns to normal in patients with hyperthyroidism after they have been subjected to subtotal thyroidectomy, and that very low galactose values are found in the blood of patients with myxedema. Determinations of absorption of galactose as an index of thyroid activity proved to be comparable in reliability to determinations of the basal metabolic rate. In clinical practice the galactose test is found to be particularly useful in patients with hyperthyroidism whose basal metabolic rates are under + 20 per cent and in patients whose basal metabolic rates are elevated owing to causes other than hyperthyroidism, such as anxiety states with hyperventilation, cardiac dyspnea and leukemia.

We have seen that only about one half of the patients with hyperthyroidism have abnormally high dextrose tolerance curves while practically all of them show abnormal elevations of the galactose tolerance curves. Since we have shown that the absorption of these two sugars is accelerated to an approximately equal degree and since we know that galactose is not immediately utilized by the tissues but must undergo conversion into dextrose in the liver, this difference is one more proof that the utilization of dextrose is increased in the hyperthyroid organism. It also makes galactose the sugar of choice for diagnostic purposes in diseases of the thyroid gland.

All peculiarities of carbohydrate metabolism in hyperthyroidism are explained satisfactorily by abnormally rapid intestinal absorption of sugars and of starch combined with increased utilization of dextrose by the tissues which leads to depletion of glycogen stores. Increased absorption of carbohydrates accounts for the "diabetic" manifestations of glycosuria, the postprandial hyperglycemia and the high dextrose tolerance curves. Chronic depletion of glycogen stores explains the low fasting respiratory quotient and leads to a compensatory acceleration of fat catabolism which, as in the case of "hunger diabetes," results in incomplete oxidation of fatty acids and brings about acidosis. Increased utilization of carbohydrate accounts for the normal or greater than normal arteriovenous blood sugar difference, postprandial rise in the respiratory quotient, and fall in the inorganic phosphates of the blood, which on the surface appear incompatible with the "diabetic" manifestations of hyperthyroidism mentioned previously. From these considerations it is also easy to see why the onset of hyperthyroidism aggravates a preexisting diabetes.

In the majority of patients with hyperthyroidism in whom diabetes is suspected, accelerated absorption of carbohydrates merely simulates certain manifestations of diabetes mellitus. However, hyperthyroidism may be superimposed on a preexisting diabetes, or the depletion of glycogen reserves and overeating, which characterize the hyperthyroid state, may in a few patients bring out a latent or a previously unsuspected mild diabetes. This explanation given by John of the increased incidence of true diabetes mellitus in patients with hyperthyroidism is supported by the observation, also pointed out by John, that the incidence of diabetes in hyperthyroidism does not rise until the beginning of the fifth decade. It may be assumed that at that age the factors precipitating a latent diabetes have exerted their influence for a longer time and that arteriosclerosis has become a contributing factor.

15. Althausen, T. L., and Stockholm, M.: Influence of the Thyroid Gland on Absorption in the Digestive Tract, Am. J. Physiol. **123:** 577 (Sept.) 1938.

16. Althausen, T. L.; Lockhart, J. C., and Soley, M. H.: A New Diagnostic Test (Galactose) for Thyroid Disease, Am. J. M. Sc. **199:** 342, 1940.

When diabetes is suspected in a patient suffering from hyperthyroidism, simple and in most cases decisive differential laboratory evidence is the fasting blood sugar, which is, of course, high in diabetes. As a rule it is normal in hyperthyroidism because there is ample time to dispose of the excess sugar in the blood following the evening meal, especially since in this condition the utilization of sugar is increased. Denis, Aub and Minot [17] emphasized that "fasting hyperglycemia is of extremely rare occurrence in hyperthyroidism." This statement is particularly significant since these authors evidently studied patients in whom the disturbance of carbohydrate metabolism was well marked, because they observed alimentary hyperglycemia (following the administration of 100 Gm. of dextrose and 50 Gm. of bread) in all their patients. Rabinowitch [18] confirmed the importance of fasting hyperglycemia in diabetes. However, a moderate elevation of the blood sugar on an emotional basis is sometimes found in nervous patients with hyperthyroidism who become excited by venipuncture, especially if several unsuccessful attempts are made before the needle enters the vein. If in such patients the determination of fasting blood sugar is repeated by a skilled operator after administration of a sedative, normal results are usually obtained. If the fasting blood sugar is still high, the presence or absence of true diabetes can be established in several ways, as pointed out by Marsh [19] and Rabinowitch. In diabetes, in contrast to hyperthyroidism, the following observations apply: (1) Glycosuria corresponds quantitatively to the intake of carbohydrates; (2) the dextrose tolerance curve shows a protracted elevation with the peak at the three hour or even four hour period; (3) the respiratory quotient remains low two hours after a dextrose meal; (4) administration of sugar does not relieve acidosis, and (5) carbohydrates have no protein-sparing action. To these may be added, as discussed previously, the decreased arteriovenous blood sugar difference and the diminished fall in inorganic phosphates of the blood following a carbohydrate meal, both of which are found in diabetes.

Several important therapeutic implications may be derived from the knowledge that the basic abnormalities of carbohydrate metabolism in hyperthyroidism consist of accelerated intestinal absorption and increased oxidation of carbohydrates. In the first place, the presence of glycosuria, postprandial hyperglycemia, or high dextrose tolerance curves in patients with hyperthyroidism does not indicate the coexistence of diabetes and can be disregarded unless there is also a high fasting blood sugar. Second, all patients suffering from hyperthyroidism should receive a high caloric diet with an abundant supply of carbohydrates. In order to compensate for the rapidity of intestinal absorption and for the increased utilization of dextrose in the tissues, it is advisable to divide such a diet into six or more meals given until bedtime. Third, patients with hyperthyroidism should not be subjected to fasting because they have a tendency to acidosis which often develops after relatively short periods of abstinence from food. This consideration is especially important just prior to operative procedures involving general anesthesia, as for instance thyroidectomy, which are a great drain on the glycogen reserves of the body in general and of the liver in particular. Fourth, intravenous administration of dextrose just before, during and after operations to patients with hyperthyroidism is valuable in lowering the operative mortality.[20] Finally, the insulinogenic mechanism of patients with hyperthyroidism who have true diabetes mellitus should be protected as much as possible from the sudden influx of large amounts of sugar after meals. This can be accomplished to some extent by omitting sugars from the high carbohydrate diet and replacing them with starch, which is absorbed more slowly (as we have shown in the table). In addition, such patients need adequate amounts of insulin. The same dietary measures may be used for prophylactic purposes in patients with hyperthyroidism who have a family history of diabetes. On the other hand, insulin should never be prescribed except in cases in which the coexistence of diabetes has been proved.

This study also contributes to a better understanding of the metabolism of carbohydrates in myxedema. It is a matter of general knowledge that dextrose tolerance curves are usually very low in patients with myxedema. In the past this was interpreted to indicate that dextrose is utilized faster than normal.[21] By studies of direct intestinal absorption in thyroidectomized rats we have shown that removal of the thyroid gland causes marked diminution of absorption of dextrose, as seen in the table. This observation was confirmed clinically by the low values of galactose in the blood of patients with myxedema following oral administration of this sugar.[16] Intravenous administration of galactose to patients with myxedema not only ruled out increased utilization of this sugar but also showed that its removal from the blood is actually slower than normal. Decreased utilization of dextrose in myxedema is in accord with other clinical and biochemical manifestations of this disease, such as a reduction in the endogenous protein metabolism and the energy exchange,[22] and probably explains why normal dextrose tolerance curves sometimes are observed in hypothyroidism in spite of decreased intestinal absorption.

No new therapeutic measures have been derived from the knowledge that intestinal absorption of carbohydrates is slowed in hypothyroidism because administration of adequate amounts of thyroid substance corrects this deficiency rapidly and effectively. Experimentally it was shown that intestinal absorption of dextrose is more sensitive to the thyroid hormone than is the basal metabolic rate; doses of thyroxine sufficient to restore normal intestinal absorption raised the basal metabolic rate only halfway to the original normal level.[23]

CONCLUSIONS

1. The basic disturbance of carbohydrate metabolism in hyperthyroidism consists of accelerated intestinal absorption of sugars and starch and of increased oxidation of dextrose in the tissues which leads to depletion of glycogen stores.

17. Denis, Willey; Aub, J. C., and Minot, A. S.: Blood Sugar in Hyperthyroidism, Arch. Int. Med. **20**: 964 (Dec.) 1917.

18. Rabinowitch, I. M.: The Glycosuria of Hyperthyroidism and Its Clinical Significance, Ann. Int. Med. **4**: 881 (Febr) 1931.

19. Marsh, P. L.: Glycosuria in Thyroid Disease, Ann. Clin. Med. **4**: 1012 (June) 1926.

20. Frazier, C. H., and North, J. P.: Carbohydrate Metabolism in Hyperthyroidism, Tr. Am. A. Study Goiter, 1933, p. 203. Frazier, C. H.: Carbohydrate Metabolism in Relation to Postoperative Crises in Hyperthyroidism, Am. J. M. Sc. **182**: 378 (Sept.) 1931.

21. Hirschl, J. A.: Osteomalacie bei Morbus Basedowi und Myxödem, Jahrb. f. Psychiat. u. Neurol. **20**: 406, 1901. Knöpfelmacher, Wilhelm: Alimentäre Glykosurie und Myxödem, Wien. klin. Wchnschr. **17**: 244, 1904. Falta, Wilhelm: Die Erkrankungen der Blutdrüsen, Berlin, Julius Springer, 1913, p. 94.

22. Means, J. H.: The Thyroid and Its Diseases, Philadelphia, J. B. Lippincott Company, 1937, p. 203.

23. Russell, J. A.: The Effect of Thyroxine on the Carbohydrate Metabolism of Hypophysectomized Rats, Am. J. Physiol. **122**: 547 (June) 1938.

2. Glycosuria, postprandial hyperglycemia and high dextrose tolerance curves in patients with hyperthyroidism do not indicate the coexistence of diabetes mellitus unless there is also a high fasting blood sugar.

3. Patients with hyperthyroidism should receive high caloric, high carbohydrate diets divided into frequent feedings.

4. Intravenous administration of dextrose is indicated just before and after thyroidectomy.

5. In myxedema, diminished absorption of carbohydrates accounts for the low sugar tolerance curves.

CLINICAL USE OF IMMUNE HUMAN PLACENTAL GLOBULIN IN CHICAGO

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In 1938 more cases of measles were reported in Chicago than during any year since this disease was made reportable. Table 1 shows that apparently there has been no reduction in the number of cases of measles reported each year over the last twenty-five years. Rather the trend is toward more cases, probably because of better reporting. The mortality, however, has dropped rather steadily from 12.4 per hundred thousand of population in 1913 to 1.1 in 1938.

It should be noted in table 1 that only the years of largest incidence are charted, one might say the epidemic years. In 1938 the case fatality was amazingly low, being 0.1 per cent, whereas in 1913 it was 1.9 per cent. However, during this year the case fatality was low over the entire country. Improved housing, more adequate medical care, better nursing attention, increased use of measles-modifying substances in susceptible contacts, recent use of chemotherapeutic drugs in pneumonias and bronchopneumonias following measles, and perhaps a lessening virulence of the type of measles prevalent in recent years may all have contributed to the reduction in the case fatality rate. Despite the reduced death rates, measles continues to take some human lives, and efforts exerted to save these lives are worth while. Until an active preventive is developed, the increased employment of measles-modifying substances should be encouraged.

In Chicago convalescent measles serum, used as a preventive and modifying substance, is prepared and distributed by the Deutsch Serum Center of the Michael Reese Hospital. Because this material is not always easily available, it was decided to study the effect of immune human globulin,[1] prepared from placental extract, among susceptible contacts. At the same time a comparative study was made with convalescent serum. The control group studied consisted of susceptible contacts who did not receive either immune globulin or serum. Table 2 shows the number of children, by age groups, receiving globulin or serum, and those not receiving any injection.

The group under 1 year consists mostly of children over 6 months of age. In every instance of a child under 6 months of age, an attempt was made to find out if the mother had had measles, because it is believed that a mother may transmit immunity to measles to the baby through the placenta and that the baby will be thus protected for five, six or seven months after birth.

In Chicago's overcrowded homes of the lower economic levels many babies do not escape measles because of their intimate exposure to the disease. Therefore every child in this group was classed as susceptible, since the entire study was made in the poorer sections of the city. Every child under observation was exposed to measles in his own family under his own roof.

METHOD OF STUDY

When measles was reported, a visit was paid to the home by a Health Department investigator, who quarantined the patient and reported the contact status. If there was no private physician in attendance, a field health officer was sent to inject globulin or convalescent serum in the contacts. In every instance possible, if there were several contacts, the health officer inoculated the younger children and employed as controls the older children in the family who gave no history of having had measles.

The health officer made a return visit some time later to note the results and to obtain as much information from the family as possible. He then completed the form shown in table 3.

The health officers engaged in this work were limited to four, so that the results are more reliable than if there were a greater number of observers.

TABLE 1.—*Cases of Measles, Deaths and Rates in Chicago, 1913-1938, Inclusive*

	Cases Reported								
	1913	1915	1917	1919	1923	1927	1929	1935	1938
	15,132	18,964	19,620	16,075	15,168	17,726	17,714	24,199	37,831
Rate per 100,000 Population	642.68	769.58	763.50	600.95	525.39	554.72	532.33	693.24	1,048.8
	Deaths								
	1913	1915	1917	1919	1923	1927	1929	1935	1938
	292	240	243	197	206	123	166	81	40
Rate per 100,000 Population	12.40	9.74	9.46	7.36	7.14	3.85	4.99	2.32	1.1

TABLE 2.—*Age Groups of Children Receiving Globulin Convalescent Serum and No Injection*

Age	Material Used		No Injection Given
	Globulin	Serum	
0-1 Yr.	418	218	14
1-3 Yrs.	212	65	115
4-9 Yrs.	45	16	186
10 Yrs. and over	3	0	13
Total	678	299	328

Table 4 shows the dosages of globulin and convalescent serum employed.

Table 5 shows the number of exposed susceptible children who received either globulin or serum and who contracted measles. For comparison, the uninoculated control group is also placed in this table.

In table 5 it is seen that serum offered 21.14 per cent greater protection than globulin, and that globulin

1. The immune globulin was furnished by Lederle Laboratories, Inc., New York.

offered 25.5 per cent greater protection than no injection. Also, it is interesting to note that 26.6 per cent of the exposed susceptible children in the "no injection" group escaped the disease even with measles in their own home.

TABLE 3.—*Information Supplied in Health Officer's Report of Measles Contact Given Globulin*

Original Patient.....
Name.....Address.....
Sex.....Age.....Color.....
Date of Onset.....Date of Eruption.....

Contacts (Include Parents)

Non-Susceptible	Name	Age
.....	.....	.....
.....	.....	.....
.....	.....	.....

Susceptible	Name	Age
.....	.....	.....
.....	.....	.....
.....	.....	.....

Contacts Injected	Dose Given	Date	Reaction
.....	.....	.....	.....
.....	.....	.....	.....
.....	.....	.....	.....

If susceptible is under 1 year, was baby breast fed?.....
Did mother of baby have measles?.....

Contacts Who Developed Measles

Name	Onset Date	Rash Date	Type of Measles	Symptoms Record from 0 to 4 Plus Rash	Cough	Catarrh	Prost.
.....	.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....	.....
.....	.....	.....	.....	.....	.....	.....	.....

Complications (if any); Give Name of Child and Describe Nature of Complications

.....
Date of all visits.....
General Remarks

NOTE: All pertinent information on every globulin assignment is to be filled in on this form when final disposition is made.

....
Date When Mailed Health Officer

Table 6 shows the number of exposed susceptible children in all three groups who contracted measles and the severity of the disease which developed, whether modified or unmodified.

From table 6 it seems that when globulin or serum was given to susceptible contacts, the two substances acted with almost equal efficiency in the doses used. Among those receiving no injections the percentage of severe cases of measles was almost two and one-half times greater than among those receiving globulin and more than three times greater than among those given convalescent serum. In this table, also, it is interesting to note that of 241 susceptible contacts not receiving any injection and who later developed measles, 76.7 per cent had it in a mild form. However, the measles epidemic of 1938 was, in general, attended with a low case fatality rate.

In table 7 are seen the figures representing both complete and partial protection afforded by globulin and serum. These figures were obtained by adding the number of children with modified measles to the number of susceptible children who did not contract the disease. A modified case of measles represents partial protection, and if a child does not develop measles it probably means complete protection. For comparison, the group receiving no injection is placed here also. In the last-mentioned group, under the heading of combined protection, are the children who did not have measles together with those who had it in a mild form.

From this table it is seen that with convalescent serum and globulin the percentage of failures to give protection is low. Among the children who received no injection, the percentage classed as failures was more than three times greater than in the globulin group.

In table 8 are recorded the complications occurring in children with measles under observation at the time of the study. Since the complications developed only in those with severe measles, these only are listed.

Table 9 shows the percentage of children who contracted measles and who remained free of rash, cough, other catarrhal symptoms and prostration.

From this table it is seen that children who received convalescent serum and later contracted measles were not as sick as the children who were given globulin and later contracted measles. The children inoculated with globulin were not as sick as those not receiving any injection. Two and six-tenths (2.6) per cent of the uninoculated children had no prostration, as compared with much higher percentages in the other two groups.

TABLE 4.—*Dosages of Globulin and Convalescent Serum Used*

Age	Globulin*	Convalescent Serum
Under 1 year	2 cc.	3 cc.
1-2 years	2¼ cc.	4 cc.
2-3 years	2½ cc.	5 cc.
3-4 years	2¾ cc.	5 cc.
4-5 years	3 cc.	5 cc.
5-6 years	3¼ cc.	5 cc.
6 years and over	.....	5 cc.

* One-fourth cc. increase in dose for each year.

TABLE 5.—*Number of Susceptible Contacts Who Contracted Measles After an Injection of Either Globulin or Convalescent Serum*

	Globulin	Serum	No Injection
Total number in group	678	299	328
Measles developed	325	80	241
Percentage of total	47.9	26.76	73.4
Measles did not develop	353	219	87
Percentage of total	52.1	73.24	26.6

TABLE 6.—*Susceptible Children in Whom Measles Developed, Showing Severity*

	Globulin	Serum	No Injection
Total number contracting measles	325	80	241
Modified or mild	293	74	185
Percentage modified	90.1	92.5	76.7
Unmodified or severe	32	6	56
Percentage unmodified	9.9	7.5	23.3

In table 10 is shown the number of children protected by globulin, according to the time interval between exposure and the giving of the injection. Table 11 shows the same for children inoculated with convalescent serum.

Before the sixth day after exposure, 181 children were inoculated with globulin. Of this number, ninety-nine, or 54.6 per cent, did not have measles. After the

sixth day of exposure, 497 were inoculated, of whom 254, or 51.1 per cent, did not have measles. Before the sixth day of exposure, ninety-three children were inoculated with convalescent serum. Of these, sixty-nine, or 74.1 per cent, did not have measles. After the sixth day of exposure, 206 were inoculated. Of these, 150, or 72.8 per cent, did not have measles.

TABLE 7.—*The Combined Protection in the Three Groups*

	Globulin	Serum	No Injection
Total number in group	678	299	328
Combined protection	646	293	272
Percentage of combined protection	95.2	97.9	82.9
Failures (including only unmodified cases)	32	6	56 (severe cases classed as failures for comparison)
Percentage of failures	4.8	2.1	17.1

TABLE 8.—*Complications*

	Globulin	Serum	No Injection
Number of unmodified cases	32	6	56
Number of cases with complications	10	2	7
Type of complication:			
Severe bronchitis	6	1	4
Otitis media	2	1	3
Severe diarrhea	1	0	0
Encephalitis	1	0	0

TABLE 9.—*Percentage of Children Remaining Free from Various Symptoms of Measles*

	Globulin	Serum	No Injection
Free from rash	1.6%	2.5%	0.0%
Free from cough	5.7%	16.25%	0.82%
Free from catarrh	17.0%	17.5%	3.3%
Free from prostration	21.1%	26.3%	2.6%

If the date of development of measles in a child in the home as given by parents is accurate, and if exposure of susceptible children is of sufficiently equal degree to make comparison possible, a higher percentage of complete protection should be expected in susceptible children receiving injections before the fifth or sixth day of exposure than after this time. However, onset dates often cannot be accurately ascertained.

It is difficult for parents to know exactly on what day measles develops in a child. In addition, there is a quantitative factor in exposure and susceptibility to measles. Many investigators have found that in a group of children exposed to measles in a hospital who receive a measles-preventive substance, there will be a higher percentage of children completely protected than in a group of susceptible children in the home who are given a measles-preventive substance. This probably occurs because in the home the susceptible child is in contact with the measles for a longer period. Contact between children is much closer in some homes than in others. These factors may help to explain why the expected results in studies made on children at home often do not materialize.

REACTIONS

Reactions from the use of convalescent serum are so unusual that in this study no attempt was made to note if any reactions occurred. On the other hand, globulin did cause reactions in many children. However, severe reactions were so uncommon that it was felt nothing could be gained from their study. The most common reaction to the globulin was a slight or moderate amount of soreness at the site of injection.

DOSAGE

The dose of globulin used in this study was smaller than that usually recommended. No doubt if larger amounts had been used soon after the exposure, more instances of complete protection would have resulted. The purpose of this study, however, was to evaluate globulin on a large scale basis, and not necessarily to determine the optimum dosage.

It has been repeatedly shown by clinical investigators that the dose of measles-preventive and modifying substances, such as immune globulin or convalescent serum, should be gaged by the following factors: (1) whether the susceptible child is in a hospital or at home, (2) the length of time following exposure, (3) intimacy of exposure, (4) the health status of the susceptible individual and (5) the type of measles prevalent.

SUMMARY

1. Six hundred and seventy-eight (678) susceptible measles contacts were inoculated with immune placental human globulin; 353, or 52.1 per cent, failed to contract measles; 325, or 47.9 per cent, contracted measles. Of the 325 children who had measles, 293, or 90.1 per cent, contracted a modified type of the disease. The number of protected children, including those who failed to have the disease plus those who had the modified type, was 646, or 95.2 per cent, of the 678 children who were susceptible measles contacts.

TABLE 10.—*Number of Days from Onset in Original Case to Injection of Globulin in Susceptible Children: Percentage of Group Protected*

Age	1 Day	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	8 Days	9 Days	Totals
Under 1 year	1/3*	5/6	7/13	28/42	38/56	49/77	32/55	39/62	67/104	266/418
1-3 years	..	2/3	3/8	7/16	6/22	13/39	10/33	13/37	17/54	71/212
4-9 years	..	..	1/2	0/1	1/9	2/4	3/9	6/11	1/9	14/45
10 years	..	..	..	..	..	..	..	2/3	..	2/3
Total	1/3	7/9	11/23	35/59	45/87	64/120	45/97	60/113	85/167	353/678
	Before Sixth Day: 99, or 54.6%, did not have measles					After Sixth Day: 254, or 51.1%, did not have measles				

* The numerator is the number of children who did not have measles and the denominator is the total number inoculated.

2. Two hundred and ninety-nine (299) susceptible measles contacts were inoculated with convalescent measles serum; 219, or 73.24 per cent, failed to contract the disease; eighty, or 26.76 per cent, had measles. Of the eighty children who had measles, seventy-four, or 92.5 per cent, contracted a modified type of the disease. Serum, therefore, offered protection to 293 of the 299 children, or 97.9 per cent.

3. Of a control group of 328 susceptible children who did not receive any injection, eighty-seven, or 26.6 per cent, failed to contract the disease; 241, or 73.4 per cent, had measles. Of the 241 who contracted measles, 185, or 76.6 per cent, had a mild form of the disease. For comparison, therefore, the protection in this group may be represented by the children not having measles plus those contracting a mild form of the disease. The protection total was 272 of the 328 in the group, or 82.9 per cent.

4. In a study of the severity of the symptoms in the measles cases occurring in all three groups, it is shown that of the group given globulin and later contracting measles, 21.1 per cent were free from prostration; of the group given serum and later having measles, 26.3 per cent were free from prostration, and of children not receiving any injection and later having measles, only 2.6 per cent remained free from prostration.

TABLE 11.—*Number of Days from Onset in Original Case to Injection of Convalescent Serum in Susceptible Children: Percentage of Group Protected*

Age	2 Days	3 Days	4 Days	5 Days	6 Days	7 Days	8 Days	9 Days	Totals
Under 1 year	4/4*	11/15	13/14	28/33	21/27	28/34	18/22	57/69	180/218
1-3 years	0/3	2/4	3/4	5/10	5/9	8/12	4/9	6/14	33/65
4-9 years	..	2/3	..	1/3	1/3	0/3	1/2	1/2	6/16
10 years	..	..	..	..	..	..	..	..	...
Totals	4/7	15/22	16/18	34/46	27/39	36/49	23/33	64/85	219/299
	Before Sixth Day 69, or 74.1%, protected			After Sixth Day 150, or 72.8%, protected					

* The numerator is the number of children who did not have measles and the denominator is the total number inoculated.

5. The time interval after exposure was studied in both the globulin-inoculated and the serum-inoculated group of children. The results obtained were not as expected. The results showed little variation whether the globulin or the serum was given before the fifth or sixth day after exposure or after the fifth or sixth day after exposure. The reasons for this are that (*a*) onset dates in measles cases occurring in homes often cannot be accurately determined; (*b*) exposure is more intimate in homes than in hospitals and is more difficult to judge in homes. Expected results, therefore, which may be obtained in hospitals, practically never materialize in the home studies.

CONCLUSIONS

In this study it has been demonstrated that placental globulin (human) can be used with great benefit in the prophylaxis of measles on a city-wide basis. When it is compared with convalescent serum, the serum seems superior, not only because it is more potent but also because reactions are uncommon. However, globulin is more readily available and in a large outbreak would have to be used because of its convenience. The optimum dosage should be determined by the physician attending the patient and the exposed susceptible children.

TRACHOMA TREATED WITH SULFANILAMIDE AND ITS DERIVATIVES

SULFAPYRIDINE AND AZOSULFAMIDE

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Sulfanilamide has been used in the treatment of various bacterial and virus infections with varying success. The causative agent of trachoma is not yet determined, but it is commonly held to be a virus. Recent papers by Loe [1] and Lian [2] report beneficial results with sulfanilamide in the treatment of trachoma. In February 1939 we started treating trachoma in the outpatient section of the Ophthalmology Department of St. Luke's Hospital No. 2 with sulfanilamide and later with its derivatives azosulfamide (prontosil) and sulfapyridine. This form of treatment of the disease is not well established, and we are presenting our observations in order that they may be added to the reports of others and evaluated, so that this form of treatment of trachoma may be placed on a sound basis.

For purpose of analysis, the cases are divided into two groups: group 1, seventy-five patients receiving sulfanilamide orally, and group 2, twenty patients receiving sulfanilamide and/or its derivatives intramuscularly. Five patients of this group were admitted to the hospital for closer observation and more detailed studies on the effects of the treatment.

GROUP 1: SEVENTY-FIVE PATIENTS TO WHOM SULFANILAMIDE WAS ADMINISTERED ORALLY

The treatment given to group 1 was carried out in the outpatient department. They came under observation every forty-eight to seventy-two hours. The patients in the clinic are mostly refugees, and a few of the more ignorant did not take the drug regularly as specified in the prescription. These did not show as rapid improvement as those who took the drug regularly.

A complete blood count and routine urine examination were done before treatment began and repeated after certain intervals when thought necessary. The patients were warned of the various toxic manifestations of sulfanilamide and told to report immediately if they became ill.

Before sulfanilamide therapy 55 per cent of the patients had had other forms of treatment in this clinic. They were treated with copper sulfate stick, 10 per cent quinine bisulfate, grattage and brossage, chaulmoogra oil, peridectomy and subconjunctival autoserum. The duration of previous treatment varied from twenty-five to 114 days with an average of two months. Many of the patients treated with sulfanilamide were chosen for this study because the former therapy had failed or the improvement was too slow.

Read before the Clinicopathologic Conference at St. Luke's Hospital No. 2, Oct. 4, 1939.

Dr. F. W. King, professor of pharmacology, St. John's University, read and corrected this paper and gave many suggestions.

Dr. F. S. Tsang, head of the Department of Ophthalmology at St. Luke's Hospital No. 2, gave us permission to study these cases.

From the Department of Ophthalmology, St. Luke's Hospital No. 2, and the Department of Pharmacology, Pennsylvania Medical School, St. John's University.

1. Loe, Fred: Sulfanilamide Treatment of Trachoma: Preliminary Report, J. A. M. A. **111**: 1371-1372 (Oct. 8) 1938.

2. Sie Boen Lian: Prontosil in Treatment of Trachoma, Geneesk. tijdschr. v. Nederl.-Indië **78**: 1058-1065 (May 3) 1938.

Symptoms and Signs of Trachoma.—The subjective symptoms most commonly complained of were, in the order of their frequency, (1) feeling of foreign body, (2) photophobia, (3) lacrimation, (4) pain or eye ache, (5) blurring of vision with marked pannus, (6) discharge, (7) blepharospasm, (8) fatigue, (9) itchiness, (10) heaviness of the lid and (11) blurring of vision without gross pannus.

The objective signs we were concerned with were congestion, papillae, follicles, pannus, infiltrations and corneal ulcers of trachomatous origin. The severity of the lesions varied from trachoma I to trachoma III and pannus from grade *a* to grade *c*.[3] In most of these cases there was trachoma II with definite papillary hypertrophy and follicle formation. In 70 per cent of the cases there was very noticeable pannus, and in twelve of them the entire corneal surface was covered by infiltration and vascularization.

Dosage.—The use of sulfanilamide in the treatment of trachoma is so new that we could find no records comparing the effects of various doses. Loe [1] recommends 0.02 Gm. per pound (0.5 Kg.) of body weight. We found this dosage sufficient in some cases but too small for continued improvement in many cases and too high in a few others. Long, Bliss and Feinstone [4] state that 5.4 Gm. of the drug is required in twenty-four hours by patients weighing from 100 to 150 pounds (from 45 to 68 Kg.) in order to establish and maintain a therapeutically effective blood level with mild or moderately severe infection. We found this dose unnecessarily high in our cases.

Most patients were started on two tablets three or four times daily depending on the body weight, which was usually between 100 and 135 pounds (45 and 61 Kg.). In a few cases it was increased to three tablets or more in each dose and in some was decreased to one tablet four times daily. The total amount of sulfanilamide necessary for improvement varied widely and seemed to have no relative relationship to body weight. One patient received a total dose of 92.7 Gm. (This large dose was given because the patient had a relapse.) Total doses in other cases varied from a maximum of 66.3 Gm. to a minimum of 19.2 Gm.

Clinical Results.—After beginning treatment with sulfanilamide, we found improvement of the subjective symptoms usually noticed after the first twenty-four to forty-eight hours. The disappearance of these symptoms varied, depending on the severity of the case. Usually those having more serious corneal involvement took a longer time to obtain relief. However, this was by no means constant. Hence some thick pannus cleared up rapidly with the disappearance of subjective symptoms, while some with slight corneal involvement required a longer time. Individual response to the drug varied widely. Most of the subjective symptoms disappeared in the latter part of the first week. The maximum time required was fourteen days for all subjective symptoms to clear up. It was found that subjective symptoms improved before improvement of the objective signs could be noticed.

Objectively, we observed that congestion of the conjunctiva became definitely less in some cases on the second or third day and in the majority of them in the first week. The beginning disappearance of follicles and papillae lags a little behind the beginning disappearance of congestion, but all cases showed definite improvement within the first ten days. Follicles and papillae definitely disappeared from the tarsal conjunctiva, the conjunctival surfaces becoming smooth with distinct blood vessels. However, slight to moderate congestion with occasional follicle and slight papillary hypertrophy still remained at the canthal regions and sometimes at the upper border of the tarsal plate. Improvement in the lower cul-de-sac was not as rapid as that in the upper lid, with congestion and thickened conjunctiva improving very slowly. Continued improvement of these residual papillae, follicles and congestion is very slow and practically imperceptible after long periods of observation—in one case after eight months.

Beginning absorption of pannus was noticed early, especially with grade *a*, in most cases in the first five days. Disappearance or marked improvement of vascularization took place in the first two weeks in practically all cases; in one case in slightly over two weeks, in one in thirty-five days and in one in forty-five days. Incidentally the last was a case of pannus crassus. In five cases sulfanilamide powder was rubbed on the lids in the same manner as boric acid powder is used to see if the congestion and residual follicles at the canthi and upper tarsal border region would disappear. In five control cases no further treatment was given. So far as can be seen, patients were not benefited by sulfanilamide rubbing. However, the subjective symptoms in one relapse improved.

Relapses.—There were one relapse during treatment and two relapses after termination of treatment. Of these three relapses, one occurred after the patient's eye had become comfortable. The dose of sulfanilamide then was reduced from six to four tablets a day. This was followed in two days by lacrimation and blepharospasm. But these symptoms subsided in two days on increasing the dose to eight tablets a day and the patient's improvement was more permanent after that.

The second patient had a relapse after 43.2 Gm. of sulfanilamide had been given, after two weeks of treatment, and he was advised to return for another week's treatment with sulfanilamide. He did not return, however, because he felt entirely comfortable. But one week later he began to have the feeling of a foreign body in his eyes and blurring of vision. Sulfanilamide was rubbed on and these symptoms disappeared subjectively in two days.

The third relapse was that of a technician who came in with trachoma II and pannus *c*. He complained of discharge, photophobia, lacrimation, blepharospasm and great impairment of vision. Under sulfanilamide treatment his eyes became comfortable in one week, and in ten days his pannus disappeared. After three weeks of treatment, the patient having taken 42 Gm. of sulfanilamide, he did not return because, he said, he was cured. A month later he returned to the clinic again with the complaint of red eyes of four days' duration and pannus *b*, corneal ulcer and all the previous symptoms present again. Sulfanilamide was given and in twelve days the condition was brought under control.

Toxic Manifestations.—Practically all our cases showed some toxic manifestations. However, when patients became too uncomfortable, stopping the drug for a day or two was all that was necessary. Toxic symptoms in the order of their frequency were dizziness, numbness of the hands and feet, anorexia, nausea, fatigue, perioral numbness, increase in bowel movements, mild skin eruption, abdominal pain, lumbar ache, pain in the jaw and pain or ache in the knee joint.

3. MacCallan, A. F.: Epidemiology of Trachoma, Brit. J. Ophth. **15**: 369-411 (July) 1931.

4. Long, P. H.; Bliss, Eleanor A., and Feinstone, W. H.: Mode of Action, Clinical Use and Toxic Manifestations of Sulfanilamide: Further Observations, J. A. M. A. **112**: 115-121 (Jan. 14) 1939.

Four patients in the series of seventy-five could not go on with the sulfanilamide treatment owing to marked anorexia, malaise and general discomfort.[5]

GROUP 2: TWENTY PATIENTS TREATED INTRAMUSCULARLY WITH SULFANILAMIDE AND ITS DERIVATIVES.

Our results with sulfanilamide given orally demonstrated to us the effectiveness of this form of treatment in trachoma. However, we experienced some difficulties and found that sulfanilamide presented the following disadvantages: 1. Large doses were necessary for improvement in most cases. 2. These large doses gave toxic symptoms. 3. Owing to irregularity or uncertainty of absorption, it was difficult to standardize the dose. 4. Many of our patients were unable to follow the directions strictly when taking the drug over a long period (three or four weeks). We searched for other methods of administration of the drug and found that Somers[6] reported that a fine suspension of sulfapyridine in distilled water given intramuscularly and intrathecally in cases of cerebrospinal fever had been successful. Kuo[7] gave it intramuscularly in 0.8 per cent sodium hydroxide in the treatment of pneumonia.

In the treatment of trachoma, in which the action of the drug should be present for three or four weeks, the formation of a drug depot in the gluteal muscles, where the insoluble substance would be absorbed very slowly and continuously, seemed rational. This form of administration presented other advantages: smaller doses could be used with less chances of toxic manifestations, and dosage could be more accurate.

Preparations Used.—We found that sulfanilamide suspended in physiologic solution of sodium chloride clogged up even our largest bore of intramuscular needles. We were unable to produce a suspension fine enough either with triturated tablets or with a pure crystalline product.

We then tried a preparation of sulfapyridine and found it very satisfactory, as it formed a milky, easily injectable suspension. The injection, however, was painful. We then used olive oil as a vehicle, adding ethyl aminobenzoate, 2 per cent giving a practically painless injection. Sulfanilamide could also be given in oil, but the clinical results were not as satisfactory as those of sulfapyridine.

Sulfapyridine and sulfanilamide were given in a 10 per cent suspension. Higher concentration gave rise to difficulty in injection. We also tried giving sulfapyridine suspended in 0.8 per cent sodium hydroxide but found that it had no special advantages over the oil preparation and was much more painful.

Therefore in most of the cases recorded in this paper a 10 per cent olive oil suspension of sulfanilamide or sulfapyridine with 2 per cent ethyl aminobenzoate was used.

Clinical Observations.—A. Cases in the Outpatient Department: Fifteen cases of trachoma were treated in the eye department with intramuscular injections of either sulfanilamide or sulfapyridine or both. In these cases no attempt was made to continue injections after subjective complaints and corneal lesions had markedly improved. These fifteen cases are subdivided into three groups according to the drugs administered.

1. Sulfanilamide. Four cases. Each injection consisted of 3 Gm. of sulfanilamide suspended in 30 cc. of olive oil.

Two cases of trachoma II*a* with pannus *a* and trachoma II*b* with pannus *c* respectively showed satisfactory improvement subjectively and objectively forty-eight hours after injection, in one case with complete ocular comfort in four days. In each there was one injection.

One case of trachoma III*a* with pannus *c* showed only moderate improvement after forty-eight hours and improvement was noticed after a second injection five days later.

2. Sulfapyridine. Nine cases. There were two cases of trachoma I, six cases of trachoma II and one case of trachoma III*b*. Except in one case, there was pannus varying from grade *a* to grade *c*. All cases but one (a case of trachoma II*b* with pannus *a*) showed marked improvement within forty-eight hours after injection, with the pannus clearing up rapidly and improvement in the palpebral conjunctival lesions more marked than in the first group.

In all these cases 3 Gm. of sulfapyridine in oil was given in each injection, and the number of injections in each case varied from one to three. Improvement progressed between injections, which were given at intervals of about seven to ten days depending on the progress noted.

3. Sulfanilamide followed by sulfapyridine. Three cases. Two cases did not respond to sulfanilamide fast enough and sulfapyridine was given a few days later, followed by marked objective improvement and disappearance of subjective complaints in ten days.

One case of trachoma III*a* with pannus *c* responded well to sulfanilamide, subjective complaints disappearing within eight days after two injections of sulfanilamide of 2 Gm. each. Two injections of sulfapyridine of 3 Gm. each were given later, and progressive improvement of condition was observed with the lids becoming pale and smooth except at the canthal regions and the cornea clear in thirty-five days of treatment.

B. Cases in the Hospital: Five patients were admitted to the hospital for more detailed and prolonged observation and for blood studies:

CASE 1.—W. A. N., a woman aged 47, weighing 138 pounds (63 Kg.), complained of blepharospasm, photophobia, itchiness, lacrimation, discharge and much pain in the left eye.

Examination showed trachoma II*b* in each eye with gelatinous confluence of follicles and a much thickened lid, which was everted only with difficulty. Congestion was moderate. Pannus tenuis was present in the right eye, covering two thirds of the cornea, and pannus crassus with connective tissue degeneration and a large, fairly deep ulcer measuring 3 by 4 mm. in the lower half of the left eye.

She was given boric acid wash in each eye three times daily, 1 per cent atropine three times daily in the left eye and one injection of sulfapyridine 3 Gm. suspended in 30 cc. of physiologic solution of sodium chloride intramuscularly on admission. Improvement was definitely noticed in thirty-six hours with the itching gone and all other complaints improved. The congested appearance of the eye was definitely better. In nine days the ulcer in the left eye was healed and the right eye completely comfortable with the pannus tenuis gone. In another week the left eye was comfortable with steady progress

5. In this connection it may be of interest to note that azosulfamide in 0.5 Gm. tablets was given to these four patients and was well tolerated. Azosulfamide tablets were also given to two other patients who had been treated with sulfanilamide and after slight initial improvement showed no further progress, even with large doses. On changing the treatment to azosulfamide they became symptom free with marked objective improvement. Two other patients were treated with azosulfamide tablets alone with very satisfactory results. Our general impression is that azosulfamide is as effective as sulfanilamide in the treatment of trachoma and may be tried when sulfanilamide is not well tolerated or when the clinical response of the patient to even large doses of sulfanilamide is not satisfactory.

6. Somers, R. B. U.: M. & B. 693 in Cerebrospinal Fever: Review of 143 Cases Treated Under Field Conditions, Lancet **1**: 921-922 (April 22) 1939.

7. Kuo, P. T.: Personal communication to the authors.

in thinning of the pannus crassus and absorption of degenerated connective tissue, leaving behind only a faint vascular remnant on the cornea thirty-five days after the first injection. After another fifteen days in the hospital the patient was discharged to the outpatient department for further observation, symptom free with the corneal trachoma healed and the tarsal conjunctiva very much thinner; only a few flat follicles and fine papillae were scattered about, mostly at the canthal regions.

TABLE 1.—*Sulfanilamide Level in Blood After Intramuscular Injection*

		Blood Level, Mg. per 100 Cc.										
		Hours				Days						
Case	Dose, Gm.	¼	1	6	12	1	2	3	4	5	6	7
1	3.0	2.69	3.37	4.34	3.47	2.00	3.68	2.00	....	....	0	0
2	3.0	....	....	....	....	2.61	1.32	1.06	0.90	0.83	Trace	....
3	3.0	....	1.48	2.01	....	....	1.11	....	0.83	....	....	Trace
4	5.0	....	....	....	....	....	1.15	....	....	0	....	....
5	3.0	....	2.08	....	....	....	1.20	....	0.77	....	....	....

CASE 2.—Y. K. M., aged 30, weighing 125 pounds (57 Kg.), complained of marked blepharospasm, photophobia, lacrimation, discharge and pain in the right eye.

Examination showed a congested palpebral conjunctiva with thickened tarsal plate and trachoma III*b*. Pannus *a* was present in the right eye with a large deep horseshoe shape ulcer distal to the pannus.

The patient was given sulfanilamide 3 Gm. in oil intramuscularly on admission, with boric acid wash and 1 per cent atropine in the right eye. In four days all complaints ceased, with disappearance of the pannus and healing of the corneal ulcer. Congestion of the palpebral conjunctiva gradually subsided and on discharge, nineteen days after admission, after two 3 Gm. injections of sulfanilamide ten days apart, the palpebral conjunctiva was pale except for some moderate congestion at the canthi with some unevenness of the surface. No definite follicles or papillae were seen; the cornea was clear of vascularization and infiltration, with the former ulcer now an excavation. Except for this optical defect the eyes felt quite comfortable.

CASE 3.—T. I. P., aged 64 and weighing 80 pounds (36 Kg.), complained of blepharospasm and photophobia in each eye with pain in the right eye.

Examination showed the palpebral conjunctiva moderately congested. In the right eye there was trachoma III*b* with pannus tenuis with infiltration taking a fluorescein stain; the left eye showed pannus vasculosus with a large deep horseshoe ulcer. Boric acid wash, 4 per cent vitamin A ointment [8] and 1 per cent atropine were given locally in each eye and 3 Gm. of sulfapyridine in oil intramuscularly on admission. In twenty-four hours there was much less pain, with the patient able to open the eyes wide and the intensity of congestion and pannus markedly reduced. Improvement progressed and the ulcer healed on the fourth day after injection. Three more days and the patient became symptom free. On the day of discharge the palpebral conjunctiva was pale and the cornea clear.

Two 3 Gm. injections of sulfapyridine were given altogether, one given in oil on admission and the second one suspended in 0.8 per cent sodium hydroxide fourteen days later.

CASE 4.—C. C. G., aged 20, weighing 120 pounds (54 Kg.), complained of photophobia, discharge, lacrimation, itchiness, fatigue, blurring of vision and the feeling of a foreign body.

Examination showed a diffusely congested thickened gelatinous palpebral conjunctiva with indistinct scarring at the upper tarsal border. Pannus grade *c* was present in the right eye and pannus grade *b* of chronic congestive type with infiltration staining with fluorescein in the left eye.

Sulfapyridine was injected on admission. The patient in the first thirty-six hours complained of increased blurring of vision with more lacrimation and pain and the infiltration getting larger. The condition, however, improved markedly the next day, with congestion much decreased and the eyes becoming comfortable six days after admission and lesions improving progressively. The pannus became very pale and sparse but refused to disappear altogether until peridectomy had been done.

Intramuscular injections of 3 Gm. of sulfapyridine in physiologic solution of sodium chloride and one intramuscular injection of sulfapyridine in olive oil were given on the first, fifth, ninth, thirteenth, seventeenth, twentieth and thirtieth day of residence.

The patient was discharged to the outpatient department after observation in the ward for thirty-eight days. The gelatinous condition of the conjunctiva was gone; a fine network of scarring was visible, and there was slight congestion at the canthal region with no definite follicles or papillae. The pannus was entirely gone and the cornea somewhat hazy from scar tissue.

TABLE 2.—*Sulfapyridine Level in Blood After Intramuscular Injection*

		Blood Level, Mg. per 100 Cc.																			
		Hours				Days															
Case	Dose, Gm.	¼	1	6	12	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1	3.0 in NaCl	3.57	2.37	2.50	3.04	3.87	2.92	2.60	2.91	2.80	3.20	2.80	2.17	1.85	1.85	0.50	0	0	0	....	....	....
2	3.0 in oil	2.17	3.11	4.71	5.00	5.23	3.94	2.95	3.04	3.33	3.12	3.25	3.07	5.72	3.25	2.50	1.50	0	....	....	....	....
	3.0 in 0.8% NaOH	2.85	2.75	3.20	3.15	2.17	2.41	2.72	2.56	2.35	3.07	....	....	....	....	....	....	....	....	....	....	....
3	3.0 in oil	....	4.50	4.40	4.00	3.80	3.37	3.19	2.61	2.40	2.80	3.07	3.40	2.90	3.31	4.54	2.50	....	....	....	....	....
4	3.0 in 0.8% NaOH	....	3.20	2.89	3.06	2.85	2.30	2.46	2.40	2.24	2.80	2.50	2.40	2.31	....	....	1.54	Trace	....	....	....	....
5	2.0 in oil	....	3.17	2.37	....	2.95	2.52	2.85	3.00	....	3.10	3.21	2.83	3.50	4.89	3.96	2.91	2.77	....	....	....	....
	2.0 in oil	....	....	....	....	....	....	....	....	2.86	....	....	....	....	....	2.73	....	....	1.90	....	....	1.38
6	3.5 in oil	....	....	....	....	2.67	2.73	....	3.00	....	3.50	....	....	....	2.47	3.68	....	....	....	....	....	....
	4.5 in 0.8% NaOH	....	....	....	....	....	....	4.66	....	2.94	....	3.75	....	3.19	....	....	....	2.75	....	....	....	2.30
7	2.0 in oil	....	....	....	....	2.46	2.30	....	2.14	....	2.70	....	....	....	....	2.50	....	....	0	....	....	....
	3.5 in 0.8% NaOH	....	....	....	....	....	4.49	....	3.68	....	2.91	....	....	....	....	....	....	2.50	....	....	....	....
8	3.0 in oil	....	....	....	....	....	....	....	....	....	....	2.40	....	....	....	....	....	....	....	....	....	....

CASE 5.—T. K. T., aged 13, weighing 63 pounds (29 Kg.), complained of lacrimation, photophobia and blepharospasm.

Examination showed trachoma II*b* with a large number of prominent follicles all over; the palpebral conjunctiva was diffusely congested. Pannus *a* was present in the right eye and pannus *b* with infiltration in the left eye.

Sulfapyridine 2 Gm. in physiologic solution of sodium chloride was given intramuscularly on admission. Within eight days the eyes became completely comfortable with the pannus entirely gone. Follicles progressively became smaller until on the day of discharge, in marked contrast to the condition of the palpebral conjunctiva on admission, no more were left on the tarsal conjunctiva and only some roughness and three or four flattened follicles with slight congestion were left in the canthal region. The lower cul-de-sac was less infiltrated but the conjunctival structures remained indistinct. Sulfapyridine injections of 2 Gm. each were given on the first, fifth, tenth, fourteenth, nineteenth, twenty-third, twenty-seventh, thirty-third, thirty-ninth, fifty-second and sixty-fifth day of residence, a total of 22 Gm. No further progress was noted after the seventh injection.

8. Ointment made from vitamin A concentrate.

Drug Reactions.—In about 80 per cent of our cases, pain and tenderness at the site of injection was noticed from six to twelve hours after injection, accompanied by fever, with a temperature ranging from 99.6 to 103 F., the former requiring from two to four days to disappear and the latter from twelve to twenty-four hours. There were in some cases headache, malaise and nausea, but only during the fever reaction. Patients complained only of some local discomfort at the site of injection but not of any of the toxic manifestations evinced by the first series of trachoma patients, who were taking sulfanilamide orally. No abscess formation ever occurred at the site of injection.

Repeated complete blood counts done in the hospital cases showed no signs of anemia, and except in one case, with a drop of 15 per cent neutrophils without leukopenia, there was no indication of danger of granulocytopenia. Hematuria did not occur.

Drug Level in Blood.—In several cases the drug level in the blood was determined according to the method of Werner [9] in an attempt to find out whether a drug depot could actually be maintained or not and to ascertain the approximate minimal therapeutic level of the drug in the blood. Data are given in terms of milligrams of total sulfanilamide per hundred cubic centimeters. The tables and the chart show the results for our hospitalized patients and some of our outpatients who were receiving the drug intramuscularly.

Dosage.—From our clinical observations and from our blood level estimations it seems to us that from 2 to 5 Gm., depending on the body weight of the patient, of sulfanilamide or sulfapyridine should be administered in each intramuscular injection. Generally speaking, for sulfanilamide one injection every four days is necessary and for sulfapyridine one injection every seven to ten days. Clinical response of the patients should be taken into consideration in determining the dose. Injection should be given until the patient is symptom free, the corneal lesions gone and the pathologic change of the palpebral conjunctiva much improved. For these results from two to six injections were all we found necessary; prolonged treatment did not give further improvement and is therefore undesirable.

COMMENT

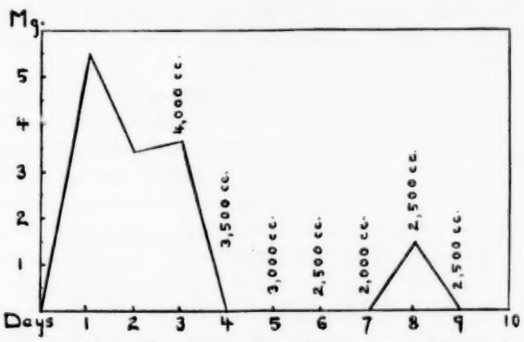
The results of our studies show sulfanilamide and its derivatives to be of definite therapeutic value against trachoma, especially in its acute stages. They act more markedly and more rapidly on the cornea as shown by the more rapid disappearance of the pannus in comparison with the follicles and papillae. The rapidity with which pannus is brought under control and ulcers healed saves the patient from otherwise increased visual disability.

From the public health point of view, as compared with other treatments, the shorter time in stopping discharge and lacrimation is very important in decreasing the chance of spread of the disease, since trachoma is most contagious when there is much discharge and lacrimation.

Our observations have shown that relapses can occur even during treatment and that an increase in dose may be necessary in these cases.

Our experience with intramuscular administration of sulfanilamide and sulfapyridine showed that sulfapyridine is more effective, probably owing to a higher and more prolonged blood level, than a similar dose of sulfanilamide (tables 1 and 2). Two patients not discussed in this paper responded much more rapidly to sulfapyridine by mouth after having had sulfanilamide orally. Sulfapyridine may have a more specific effect on the trachoma virus, although more study is necessary to enable us to draw a definite conclusion.

Long [10] warned against the intramuscular administration of an oil preparation of sulfanilamide on the grounds that with a severe reaction rapid elimination of the drug would be impossible. However, in all cases in which severe toxic reactions have been reported,[11] much larger doses in a shorter period of time have been used, consequently with a much higher blood level as compared with the amount suggested by us. Besides, as shown in the chart, the drug level in our cases could be depressed to zero by forcing fluid. We think therefore that, with the small amount of drug used and the ease by which the drug level could be lowered, administration by intramuscular injections of sulfanilamide or sulfapyridine in oil is as safe as oral administration if not more so because of slower absorption and is much more economical.



Level of sulfapyridine in the blood of a patient given 4 Gm. intramuscularly, followed by forced fluids begun on the third day. The drug level is given in milligrams per hundred cubic centimeters and the amount of fluid in cubic centimeters administered in twenty-four hours.

SUMMARY AND CONCLUSIONS

1. Studies on treatment of trachoma with sulfanilamide and its derivatives administered orally to seventy-five patients and intramuscularly in the form of a fine suspension in oil to twenty patients were made in St. Luke's Hospital No. 2.

2. They were found to be definitely effective against trachoma in stages I, II and III, being most useful in eliminating subjective complaints and in checking and healing pannus and corneal ulcer. Pathologic conditions in the palpebral conjunctiva were improved markedly but always remained in the canthal regions. The upper and lower cul-de-sac were not much influenced by prolonged oral or intramuscular administration of the drugs.

3. Intramuscular administration of sulfanilamide suspended in oil and especially of sulfapyridine has, besides the therapeutic effectiveness of the oral administration, the advantage of prolonged action, decreased dosage, lack of toxic manifestations and increased ease in con-

9. Werner, A. E. A.: Estimation of Sulfanilamide in Biological Fluids, Lancet **1**: 18-20 (Jan. 7) 1939.

10. Long, P. H.: Oily Suspension of Sulfanilamide, Lancet **1**: 60 (Jan. 7) 1939.

11. Coxon, R. V., and Forbes, J. R.: Agranulocytic Angina Following Administration of M. & B. 693, Lancet **2**: 1412 (Dec. 17) 1938. Barnett, H. L.; Hartmann, A. F.; Ferley, A. M., and Ruhoff, M. B.: Treatment of Pneumococcic Infections in Infants and Children with Sulfapyridine, J. A. M. A. **112**: 518-527 (Feb. 11) 1939. Johnston, F. D.: Agranulocytosis Following Treatment with M. & B. 693, Lancet **2**: 1200 (Nov. 19) 1938. Sutherland, M. E.: Agranulocytosis Following Administration of M. & B. 693, ibid. **1**: 1208 (May 27) 1939. Shecket, H. A., and Price, A. E.: Fatal Granulocytopenia Following Administration of Sulfanilamide, J. A. M. A. **112**: 823-828 (March 4) 1939. Harvey, A. M., and Janeway, C. A.: Development of Acute Hemolytic Anemia During Administration of Sulfanilamide (Para-Aminobenzenesulfonamide), ibid. **109**: 12-16 (July 3) 1937.

trolling and managing patients. The disadvantage lies in the pain and transitory fever the injection causes, although they are never severe enough to incapacitate the patient.

4. Blood estimations show that sulfanilamide admintered intramuscularly is present in the blood for approximately four days, while sulfapyridine remains in the blood from ten to fourteen days, whether they are suspended in physiologic solution of sodium chloride, olive oil or 0.8 per cent sodium hydroxide. The minimum therapeutic level appears to be between 2 and 2.5 mg. per hundred cubic centimeters.

5. In the oral administration of the drug, the daily dose of 0.02 Gm. per pound of body weight may be used in all cases with the reservation that it may be either increased or decreased during the course of treatment according to the clinical response of the patient; slow or no response of some patients to the drug may be corrected in practically all cases by increase in the dose. In a few cases, changing to azosulfamide or to sulfapyridine proved effective. The duration of treatment varied from two to four weeks.

In the intramuscular administration of the drug, the dose is from 2 to 5 Gm. per injection, depending on the weight of the patient, sulfanilamide being given every four days and sulfapyridine every seven to ten days. From two to six injections are all that are necessary; more are undesirable, since improvement further than that just described has never been observed.

37-B Brenan Road.

LYMPHOSARCOMA

A STUDY OF 196 CASES WITH BIOPSY

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AND
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(Concluded from page 23)

TREATMENT

It was but part of a natural course of events which caused irradiation to supplant surgical methods almost entirely in the treatment of lymphosarcoma, for in no other tumor process is there so startling a response to this mode of therapy. In general lymphosarcoma is extremely radiosensitive, and it is not surprising to observe a bulky tumor mass regress to half its size after a few days of treatment and completely disappear within a week. Recurrences in areas adequately treated rarely occur, the new evidence of disease being found elsewhere.

With several types of irradiation available at the Memorial Hospital, various methods of treatment and their combinations have been employed over a twenty year period. Forty-nine per cent of the patients were treated by x-rays alone generated at from 140 to 200 kilovolts. Target-skin distances varied from 35 to 100 cm., depending on the depth of the tumor beneath the skin surface. Filtration also varied considerably from none at all to 0.5 mm. of copper. The area of any field treated was uniformly planned so as to encompass well the tumor known to be present, no attempt being made in a routine way to apply so-called prophylactic treatment to adjacent, clinically uninvolved node groups or tissue with the purpose of destroying embolic deposits presumed rather than known to be present.

Dosage has been purposely varied from 100 to 800 roentgens per individual treatment, the interval between treatments being roughly proportional to the size of the single dose to allow for skin recovery and varying, therefore, from one to seven days. The total amount delivered to any area was determined as treatment proceeded by the rate and degree of tumor regression as well as by the condition of the skin. Twelve per cent of patients were treated by radium element or radon. In the majority of these the 4 Gm. radium element pack was used at from 6 to 10 cm. distance. In an occasional instance this was supplemented by interstitial implantation of gold-filtered radon seeds. Individual treatments varied in amount from 4,000 to 10,000 milligram hours, the same considerations maintaining as in using x-rays with regard to the time permitted to elapse between treatments and the total dose transmitted to any given area. Thirteen per cent of patients were given both x-rays (from 140 to 200 kilovolts) and the radium element pack treatment.

Any disease in which the rapidity and extent of growth may vary so markedly and whose manifestations are so protean requires the strictest individualization of treatment. Consequently, no definite pattern for the management of these patients can be laid down. In an attempt to convey an approximate idea of what has been done, however, the course of the entire group has been calculated on the basis of averages. It is hoped that the amalgamation of such a large number of proved cases as is here presented may justify this otherwise dangerous and frequently misleading procedure, and it must constantly be borne in mind that only in the most general sense can such figures be applied to individual cases.

A hypothetic average patient therefore received a total of twenty-four treatments (x-rays, element pack, or both) with an average interval of two or three days between them. These twenty-four treatments were given in an average of three separate courses, with an interval of about thirteen weeks elapsing between two successive courses. It might here be repeated that the principle determining a new course of therapy was in all instances clinical evidence of recurrent or metastatic disease and that in no instance was prophylactic treatment given. Therefore the number of courses reflects the activity of disease in the average case rather than a degree of ambition in applying treatment. Such a course might consist of a single or several treatments to one or more areas. The total number of areas treated averaged six or seven, with about four treatments per area. In respect to dosage, the average patient received a little more than 400 roentgens [10] per treatment, about 1,600 roentgens per area, and about 3,500 roentgens per course. The average radium treatment consisted of from 7,000 to 7,500 milligram hours, each area receiving about 35,000 milligram hours, and about 40,000 milligram hours constituting the average dose per course.[11]

Eleven per cent of the patients received Heublein total radiation treatment. The average dose per treatment in the entire group was 125 roentgens. This form of therapy was usually reserved for those with generalized lymphosarcoma or for those in whom the disease by its aggressiveness threatened soon to become widespread. Therefore in later judgment of this form of treatment consideration must be given to the unfavorable type of disease assigned thereto.

10. This represents roentgens in air and not tissue dosage.
11. The much smaller number of cases in this group (twenty-one) makes any generalization very uncertain.

Surgical therapy was initially employed in 15.3 per cent of cases, with the intention of thereby effecting a cure. It consequently follows that any patient for whom surgical treatment became necessary as a result of disease complication such as intestinal obstruction is not included in this group. It also follows that in each of the cases just cited the surgical procedure was extirpative in type, as much of the tumor being removed as was possible when complete removal could not be accomplished. This involved either excision of an extranodal primary lesion or a node dissection or both.

TABLE 4.—*End Results in Lymphosarcoma After Five Years or More*

Total number of cases		196
Indeterminate group		
Dead of other causes without recurrence Lost track of without recurrence		6
Patients dying of disease 1934-1938 *		58
		64
Determinate group		
Total number minus indeterminate group		132
Failures		
Dead of lymphosarcoma Lost track of with disease		111
Successful results		
Patients surviving 5 or more years		21 (15.9%)
End results after five years		
Patients dying of disease or living with recurrence after 5 years		7 (5.3%)
Patients living and well after 5 years (apparently cured)		14 (10.6%)

* Indeterminate only from standpoint of five year end results.

About one fifth of the surgically treated patients received no other form of therapy. The remainder all received postoperative external irradiation, either radium or x-rays, given regardless of the absence of clinical disease. This might be regarded then as the only type of case in which prophylactic irradiation was given. Five and five tenths per cent of patients received injections of erysipelas and prodigiosus toxins (Coley [11a]) supplementary to irradiation, operation or both.

Transfusions were resorted to when anemia or leukopenia became marked following irradiation, the rationale being simply to tide the patient over a critical period when diminished resistance might throw wide open the door to a fatal infection. This occasionally appeared to be quite successful. In instances, however, in which the disease has become uncontrollable and is rapidly advancing, blood infusion becomes simply a gesture and has no practical value.

PROGNOSIS AND RESULTS OF TREATMENT

Adopting the method of reporting end results suggested recently by Martin, with slight modifications (tables 4 and 5), there are in the determinate group 132 patients of whom twenty-one have survived five or more years, a five year survival rate, therefore, of 15.9 per cent. Desjardins and Ford reported an 11 per cent five year survival rate in 1923. Of our survivors fourteen (10.6 per cent) are living and are apparently cured, five (5.3 per cent) died of their disease at least five years after treatment, and two are living with active disease still present. Reports of from 30 to 35 per cent five year cases (Leucutia,[12] Jutras [13]) with the present day methods of treatment are open to question. A more critical review of pathologic material might well reduce such optimistic figures.

In the course of studying the entire group of cases here presented it became strikingly apparent that probably the single most important factor determining success or failure in lymphosarcoma lay in some inherent quality of the disease which as yet it is impossible to evaluate. The histologic picture, so helpful in prognosticating the course of many tumors, is of little aid here. One cannot predict on the basis of histology which of two clinically similar cases is apt suddenly to become generalized and which will remain localized for a considerable period. In carefully reviewing the microscopic slides of cured patients no explanation for their favorable outcome could be obtained; in fact several presented as wild a picture as could be imagined. In general the giant follicle lymphomas run a less rapid course, one of nine patients being alive and well and the remainder having survived for an average of forty-two months (more than twice that of the general group). Of the patients having tumors of the small cell type (malignant lymphocytoma) none are living but the average duration of life was 18.6 months (about the same as that of the general group).

The clinical setting is slightly more helpful. Of the twenty-one patients surviving only four had more than two contiguous areas of involvement at the time of admission, so that it may be stated that survivals will probably be secured from the group arriving with clinically early disease. However, of patients eventually dying from disease, those whose disease was considered early at the time of admission (one or two areas of involvement) outlived those who were considered to have generalized involvement (three or more areas) by only one month.

TABLE 5.—*Summary of Patients Surviving Five Years or More (Twenty-One)*

1. Incidence:			
Sex: Males	11		
Females	10		
Age (average)	46 years		
2. Average duration of symptoms before treatment			12.0 months
3. Extranodal primary			9 cases—(43%)
(Involving one of the head structures)			8 cases)
4. Average number of areas involved on admission			1.5
(4 patients had 3 or 4 areas involved)			
5. Prognosis Table:			
Determinate group			132 cases
Five year survivals			21 cases—(15.9%)
Apparently cured after 5 years			14 cases—(10.6%)
Died of disease after 5 years			5 cases—(4.4%)
Living with disease			2 cases—(1.5%)
6. Treatment:			
Surgical alone	1	All living and well	
Surgical plus irradiation	5		
X-rays alone	11	6 died of disease; 5 living and well	2 had supplementary Heublein
Radium alone	0		
X-rays plus radium	4	1 died of disease; 3 living and well	
	21		
7. Main Treatment Factors:			
Average roentgens per treatment			410
Average roentgens per area			1,770

When the disease begins in one of the cranial structures the prognosis appears to be somewhat better, twenty-three per cent of patients surviving five or more years and 15.4 per cent being apparently cured.

The occasion of a primary site in the gastrointestinal tract, regardless of sporadic reports of cures, seems to carry with it an unfavorable outlook. None of the

11a. Coley, W. B.: End Results in Hodgkin's Disease and Lymphosarcoma, Treated by the Mixed Toxins of Erysipelas and Bacillus Prodigiosus, Alone or Combined with Radiation, Ann. Surg. **88:** 641 (Oct.) 1928.

12. Leucutia, Traian: Irradiation in Lymphosarcoma, Hodgkin's Disease and Leukemia, Am. J. M. Sc. **188:** 612 (Nov.) 1934.

13. Jutras, Albert: Protracted Roentgen Therapy of Pharyngeal Lymphosarcoma, Am. J. Roentgenol. **39:** 792 (May) 1938.

patients whose stomach or small intestine was involved lived five years, the average survival period being 6.6 months.

Of the patients in whom a leukemic or pseudoleukemic blood picture was superimposed none survived five years, but the average survival from time of onset until death was 24.2 months, no shorter than for the lymphosarcoma group as a whole.

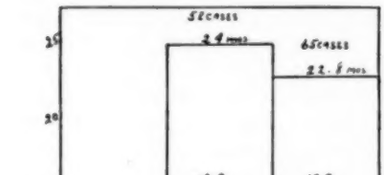

Fig. 10.—Influence of age on the course of the disease, the relatively greater influence of treatment in patients over 30 years of age and the average life span from onset of symptoms till death. The average duration of symptoms until initiation of treatment (shaded) was 8.7 months for all ages. The average duration of treatment until death (white) was 11.8 months for all ages. The average duration of the disease was 20.5 months.

The age of the patient appears somehow to exert considerable influence on the subsequent course (fig. 10), those under 30 years of age tending to experience a much more acute course and having about half the life expectancy of those over 30. After 50 years of age the life expectancy drops off somewhat, probably as a result of the increasing influence of complicating degenerative systemic changes. Since quantitatively treatment was about the same for all of these age groups, the explanation must be in the disease itself. The average age of the patients surviving five or more years was 46 years, about the same as that of the entire group. Only a single patient under the age of 30 survived.

It would appear to be a matter of the utmost importance in any disease offering so dismal an outlook to attempt to form some practical opinion of the relative worth of the several methods of treatment employed (table 6). Of sixty "determinate" patients treated by x-rays alone nine, or 15 per cent, survived five or more years. Five of these (8.3 per cent) are apparently cured; two subsequently died of disease and two are living with disease still present. Four (19 per cent) of twenty-one patients treated by both x-rays and radium (interstitially or by element pack) survived five years, but one later died of disease. Of seventeen patients treated by means of the 4 Gm. element pack alone, none have survived five years. There were ten determinate patients who received Heublein whole body irradiation following initial local irradiation or surgical treatment and of these two survived five years but eventually died of disease.

In summary, then, 108 patients were treated by some method of irradiation of whom fifteen (13.9 per cent) survived five or more years but of whom only eight (7.4 per cent) are apparently cured.

Twenty-five determinate patients were initially subjected to some extirpative surgical procedure: removal of an extranodal primary site (such as tonsil, breast or ileum) in eleven; node dissection in twelve, and removal of both an extranodal primary and an adjacent involved node group in two. With all but a few of these patients surgical treatment was shortly followed by local external irradiation given prophylactically. Of these patients six (24 per cent) are living five or more years later and all are apparently cured. A group of sixty-two patients on admission were considered to have a comparable amount of clinical disease, though in some instances not as anatomically accessible, and were treated by some form of radiation. Of these 16 per cent survived five years but only 8 per cent are apparently cured. The small size of these two groups prohibits any definite conclusions but certainly encourages further trial of a combined surgical and radiologic approach in these early cases.

It should be pointed out that many of the surgically treated patients were operated on in smaller hospitals by surgeons who were first aware of the prevailing condition after the pathologic report on the tissue removed had been made. Thus it seems safe to assume that in several instances at least the procedures were not as radically done as they might have been had the diagnosis been previously known or at least strongly suspected, and one is tempted to speculate, therefore, whether or not these surgical results could not be improved on. At any rate it would appear that more attempts to treat patients in the early stage (when there is reason to believe that the disease still remains localized to a single area or to not more than two associated and contiguous areas) by surgical means are worthy of trial.

A far greater problem than the choice of initial treatment for patients with incipient lymphosarcoma is the program to be followed in treating those in whom the disease has already become advanced, either because of its inherent fulminating character or because of neglect or unsuccessful initial treatment. Few of these patients can be expected to survive even five years, and practically all will eventually die of their disease or some complications attributable to it. It might be reiterated here that only four patients having three or more areas of involvement survived the minimum five year period. One of these was lost track of after seven years apparently free from disease, but the remaining three eventually died of it.

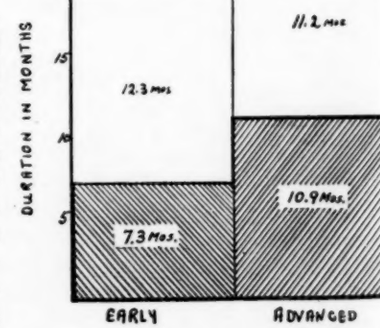

Fig. 11.—Relation of extent of clinical disease on admission to duration of life in patients dying of lymphosarcoma. The average duration of symptoms until initiation of treatment (shaded) was 8.7 months for all patients. The average duration of treatment until death (white) was 11.8 months for all patients. The average duration of the disease was 20.5 months.

Desjardins in 1923 frankly stated that he questioned the efficacy of roentgen therapy in prolonging life. It is assumed that this excepts those cases in which life is immediately threatened by the occurrence of mediastinal compression, intestinal obstruction or some other acute complication.

Minot and Isaacs in 1926, reporting on lymphoblastoma, produced figures showing a slightly longer survival of treated as compared with untreated patients, 2.88 and 2.45 years respectively. They concluded that treatment was of some benefit in cases destined to experience an acute course but was probably without influence on disease of a more chronic nature.

Since all but two of the patients in the present series received some form of therapy, it was impossible to compare palliative results as measured by duration of life in treated and untreated groups. However, it seemed reasonable to suppose that some idea of its value might be obtained by comparing results for patients appearing with incipient disease with results for those whose disease might be considered well advanced by the time treatment was sought. In selecting these two groups the extent of clinically demonstrable disease at the time of admission was used as the criterion, those presenting either a single involved area or two adjacent sites of disease being designated as "early" and all others as "advanced."

TABLE 6.—*Relationship of Type of Treatment to the Number of Patients Surviving Five Years or More*

Type of Treatment	Total Cases	Indeterminate	Determinate	5 Year Cases: Survivals	5 Year Cases: Apparent Cures
X-rays alone	96 (49%)	36	60	9 (15.0%)	5 (8.3%)
X-rays plus radium	26 (13.3%)	5	21	4 (19.0%)	3 (14.3%)
Radium alone	23 (11.7%)	6	17	0	..
Heublein alone or combined with radiation or surgery	22* (11.2%)	12	10	2 (20.0%)	0
Irradiation, all types	167 (85.2%)	59	108	15 (13.9%)	8 (7.4%)
Surgery alone or combined with radiation	30 (15.3%)	5	25	6 (24%)	6 (24%)
No treatment (far advanced disease)	2 (1%)	..	2	0	..
Total	196 (100%)	64† (32.5%)	132 (67.5%)	21 (15.9%)	14 (10.6%)

* Three cases also included in the 30 cases treated surgically.
† Fifty-eight of these are patients admitted 1934-1938, now dead of disease.

If treatment were of definite value in prolonging life one should logically expect that patients first seen with clinically early disease would have a much longer course than those whose treatment was instituted at a time when the disease appeared to be well under way. In other words, the survival of the early patients from beginning of treatment to death should be appreciably longer than that of the advanced patients. Actually there was very little difference (fig. 11), the early patients surviving 12.3 months and the advanced 11.2 months from the beginning of treatment. It was found, moreover, that the period of survival from onset of symptoms to application for treatment was 7.3 months in the early group as compared with 10.9 months in the advanced group. The total duration of the disease, therefore, from onset till death was 19.6 and 22.1 months respectively, a difference of 2.5 months (11 per cent) in favor of those whose disease was considered advanced on admission. It would seem, therefore, that the natural course of events had been either entirely unaffected or slightly hastened by treatment.

It might be recalled at this point that several forms of treatment and their combinations were employed and that the figures just cited represent a net average. A determination of the relative merits of each method consequently becomes imperative. This proved to be quite interesting (fig. 12).

Of all patients who eventually died of their disease, those treated with the element pack responded worst and survived only 6.4 months from the beginning of treatment; those who received x-rays and radium reacted somewhat better and lived 9.6 months; those on whom x-rays (from 140 to 200 kilovolts) alone were employed lived 12.5 months; patients treated surgically with postoperative irradiation, usually x-rays, survived 12.3 months, and patients who received whole body irradiation (Heublein) supplementary to local irradiation lived 18.2 months from the time treatment was begun. This very orderly progression is difficult to explain but is so definite that it must be considered.

The group receiving a known amount of x-rays alone was the largest (seventy-nine patients) and could with some degree of accuracy be still further broken down. In addition, patients were included at least 75 per cent of whose treatment had consisted of this type of irradiation, forming a composite group of 114 cases. On subdividing these on the basis of size of the average treatment (fig. 13) it was found that patients receiving from 400 to 600 roentgens did best with a survival from start of treatment to death of 17.3 months as compared with 10.3 months for those receiving from 100 to 300 roentgens, 11.9 months for those given from 300 to 400 roentgens and 10.4 months for patients given average doses of from 600 to 800 roentgens. Thus it would appear that the small doses probably have too little killing effect on the disease, that the very large doses exert too marked an effect on the patient and that the intermediate doses probably bring about some compromise between the two. The average dose delivered per area also seemed to exert some influence on the duration of life (fig. 14). Patients receiving 1,000 roentgens or less per area survived only 11.6 months from the time of beginning treatment, whereas those receiving from 1,000 to 2,000 roentgens per area survived 14.1 months, those given from 2,000 to 3,000 roentgens 14.9 months, and those receiving 3,000 roentgens or more 13.1 months. It is naturally often impossible to attain a dose of from 2,000 to 3,000 roentgens per area in patients with widely disseminated disease, but it would seem advisable to strive for this in those whose disease is apparently restricted to several areas and whose good state of general health will permit. Because prophylactic irradiation is in general not given at this hospital except as an adjunct to surgical therapy, the average treatment per course can merely reflect the inherent aggressiveness of the disease and adequacy

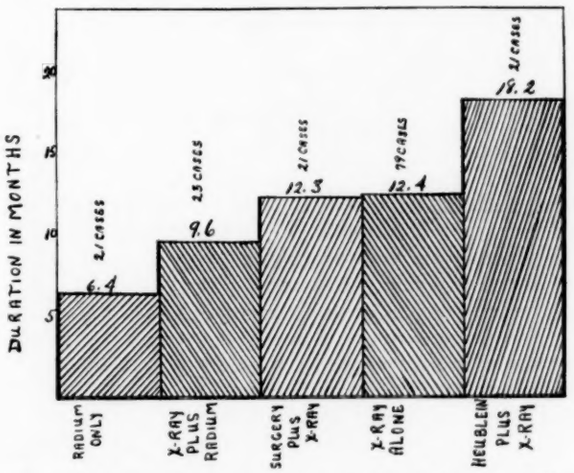

Fig. 12.—Relationship of type of treatment to the duration of life from the institution of treatment till death (average of all cases, 11.8 months).

or inadequacy of previous treatment in controlling it. The former remains an unknown factor and the latter has already been presented.

SUMMARY AND CONCLUSIONS

The etiologic and clinical features and the results of treatment of 196 histologically proved cases of lymphosarcoma at the Memorial Hospital since 1918 were

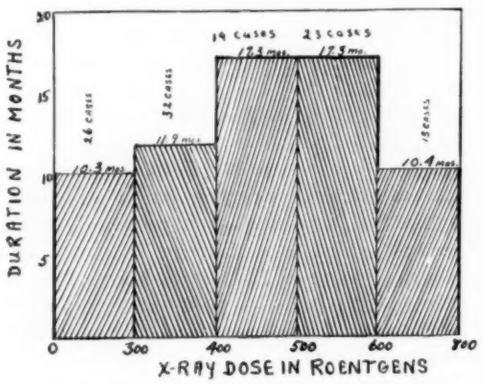

Fig. 13.—Relationship of the average dose per treatment to the duration of life in months (average of all cases, 11.8 months).

studied. Nine cases of giant follicular lymphoma were included, as that condition is here regarded as a type of lymphosarcoma. Hodgkin's sarcoma was excluded from this study.

The etiology of lymphosarcoma remains obscure. It is worthy of note that in 32 per cent of cases in which the first symptom was cervical lymphadenopathy there had been or was present definite chronic infection of the upper respiratory tract. The disease appeared to begin in the majority of instances as a local process and to spread mainly by cell emboli but perhaps also by the diffusion of some activating agent. It also seems possible that in some cases there were multiple foci of origin.

The age and sex distribution were as follows: Extremes of age were 4 and 88 years, with rather uniform distribution by decades, not more than 27 per cent of cases falling within any one decennium (from 50 to 59 years). The average age for both males and females was 45 years. The ratio of males to females was 7 : 3.

Reticulum cell lymphosarcoma was by far the most common type, accounting for 184 cases. Giant follicular lymphoma was diagnosed in nine cases. There were three cases of malignant lymphocytoma.

The early stages were characteristically free of constitutional symptoms and were signalized by the discovery solely of external lymph node enlargement in 65 per cent of cases. Abdominal symptoms were first noted in 17.5 per cent, upper respiratory tract symptoms in 11.6 per cent, thoracic symptoms in only 3.6 per cent and bone pain in 1.8 per cent.

As far as the records in this series show, lymphosarcoma most commonly begins and runs its early course only in lymph nodes. Two thirds of this series of patients never showed evidence of an extranodal primary lesion. In the one third in whom an extranodal primary lesion was found, it was located in one of the structures of the head and neck in 65 per cent, chiefly in the tonsil and nasopharynx. In 16 per cent the extranodal primary lesion appeared in the gastrointestinal tract, and in the remaining 19 per cent the primary lesions were miscellaneous and widely scattered.

The following were the sites of the first nodes found to be enlarged: neck 59 per cent, axillas 11.4 per cent, groins 11.9 per cent, abdomen 13.1 per cent, mediastinum 1.1 per cent and epitrochlear region 0.5 per cent. In 2.8 per cent (five cases) practically the entire node system appeared to be affected simultaneously.

According to the extent of the disease on admission, cases were classified as follows: (1) no evidence of disease (because of recent surgical removal) 3.6 per cent, (2) only one area affected 40.2 per cent, (3) two contiguous areas affected 12.5 per cent and (4) three or more areas affected 43.8 per cent.

Though early extension generally involves contiguous node groups, later involvement of distant organs is most reasonably explainable by the hematogenous route. The spleen was palpable in 21 per cent of cases (compared with 45 per cent in our Hodgkin's disease series). The liver was palpable in 8 per cent (Hodgkin's disease 24 per cent). Pleuropulmonary disease was shown roentgenographically in 12 per cent (Hodgkin's disease 29 per cent). Osseous lesions were found in 9 per cent (Hodgkin's disease 24 per cent). Metastatic skin lesions occurred in 5.5 per cent.

Anemia is in general slower in developing in lymphosarcoma than in Hodgkin's disease. There is no characteristic blood picture for lymphosarcoma. With the exception of 6.6 per cent of cases in which a more or less typical leukemic blood count was found, the differential count in general showed a predominance of cells of the granulocytic series.

The various methods of treatment employed included x-rays (from 140 to 200 kilovolts), radium (mainly the 4 Gm. element pack), x-rays and radium combined, Heublein total irradiation (usually combined with local external irradiation) and surgical extirpation (generally followed by local irradiation). So-called prophylactic irradiation was not carried out except as a supplement to initial surgical therapy.

Results of treatment were as follows: In a determinate group of 132 cases there was a five year survival rate of 15.9 per cent; 10.6 per cent of the patients are living after five years or more and are apparently cured.

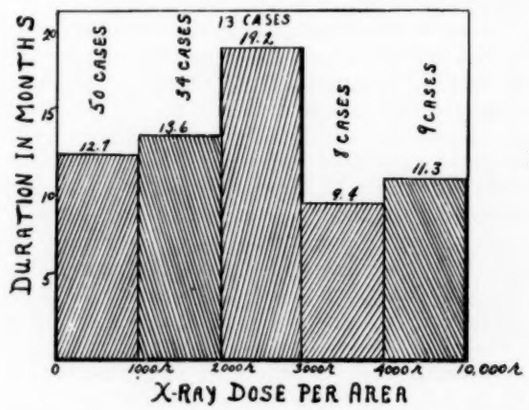

Fig. 14.—Survival from beginning of treatment till death as related to the average dose per area (average of all cases, 11.8 months).

Of the twenty-one patients showing a five year survival, only four had more than one area affected initially.

Among the factors influencing the course of the disease are (1) its individual inherent qualities for growth and dissemination, probably most important though least definable, (2) the extent of disease on admission, (3) location of the primary lesion, (4) complicating pseudoleukemia or leukemia and (5) the age of the patient.

Analysis of the results of treatment suggests that (1) for clinically early (single area of involvement) and easily accessible disease radical surgical removal followed by prophylactic external irradiation is at least worthy of serious consideration and further trial and (2) for the more advanced stages of the disease either local roentgen irradiation plus total roentgen irradiation or local roentgen irradiation alone is superior to local roentgen plus radium pack irradiation or radium pack irradiation alone.

A study of roentgen dosage in relation to results suggests that divided dose therapy, using single doses in the order of from 400 to 600 roentgens and total doses per field in the order of from 2,000 to 3,000 roentgens, yielded the best results.

York Avenue at Sixty-Eighth Street.

EXTRAGENITAL TRANSMISSION OF SYPHILIS AMONG FIVE PERSONS IN ONE FAMILY

A CASE REPORT

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AND
JAMES ROBERT HENDON, M.D.
LOUISVILLE, KY.

Report of these five cases of syphilis is made because of many unusual features involved. Infections with Spirochaeta pallida due to husband-wife transfer are not uncommon nor is congenital syphilis by any means a rarity. There have been, however, no reports of multiple infections within one family identical with the study outlined here.

REPORT OF CASES

On Oct. 16, 1939, Mrs. E. X brought her daughter Paula, aged 18 months, to the surgical dispensary of the Louisville City Hospital because of a sore on the baby's lower lip. This had appeared from six to eight weeks previously. The child had been taken to a physician, who diagnosed the lesion as one of impetigo and prescribed an ointment. In spite of the use of this preparation the lesion had persisted and progressed, and approximately four weeks later the child's body had been covered with a reddish rash which faded after seventy-two hours.

At the initial examination of the patient in the surgery there was seen a pinkish discoloration of the lower lip on the right involving the mucous membrane and extending downward. This area measured 2.5 by 1.5 cm.; there was no discharge and no break in the continuity of the skin. Beneath the skin in this area was an indurated mass which was not tender. No additional lesions were seen within the mouth, although the tonsils were markedly hypertrophied. There was enlargement of the anterior cervical glands bilaterally, and there was generalized lymphatic enlargement of a lesser degree. A small crusted ulcer was present on the anterior skin fold of the left axilla. The observations were otherwise not remarkable.

Syphilis being suspected by the surgeon, the child was referred to the diagnostic clinic. Here a dark field examination of material from the axillary lesion was attempted but was unsuccessful. The blood Kahn reaction was strongly positive. The diagnosis was secondary syphilis with extragenital primary source.

An epidemiologic study of the entire X family, including a boarder in the home, was immediately made. This study included a careful history and physical and serologic examination of each member.

From the Division of Venereal Disease Control, Louisville Department of Health.

The following disclosures were made:

Mrs. E. X, the mother, was nonsyphilitic.

Mr. H. X, the father, was nonsyphilitic.

R. X, a son aged 15, was nonsyphilitic.

J. A. X, a son aged 8, was nonsyphilitic.

J. X, a son aged 4, was nonsyphilitic.

H. X, a boarder aged 23 and no relation, was nonsyphilitic.

Jess X, a daughter aged 11, had a discharging indurated nontender ulcer on her lower lip (fig. 1). This had appeared about three weeks previously (three weeks after appearance of the primary lesion on Paula's lip). Jess's anterior cervical glands were enlarged; others were not palpable. A dark field examination of material from the lesion on the lip was positive for Spirochaeta pallida. The diagnosis was primary syphilis.

Charles X, a son aged 6, had a fissured encrusted lesion between the pinna of the left ear and the head (fig. 2). There was general lymph gland enlargement, and the body was covered with ham-colored macules less than 1 cm. in diameter. A dark field examination of material from the ulcer was positive for Spirochaeta pallida and the blood Kahn reaction was strongly positive. The diagnosis was primary and secondary syphilis.

Valerie X, a daughter aged 17, had a superficial white excoriation about 5 mm. in diameter involving the mucous membrane inside the lower lip. There were two small vesicles on the external surface of the lip. The pharynx was inflamed; the tonsils had been extracted. The cervical glands were enlarged bilaterally. The blood Kahn test was strongly positive. There had been no history of any earlier lesions on the mucous membranes or on the skin. The diagnosis was secondary syphilis.

Two blood Kahn tests made on Clark X, a son aged 19, were strongly positive. He was unaware of any history of

Fig. 1.—Primary syphilitic lesion of lower lip of child aged 11.

a primary lesion or of secondary lesion but later recalled that he had had a severe sore throat in June or July 1939. The symptoms were described by him as being associated with yellowish blisters on the back of the tongue and on both tonsils. He was seen at that time by a physician, who pronounced the condition to be trench mouth and prescribed a gargle. After about ten days the subjective symptoms subsided. Immediately after this he noted that reddish areas of various sizes appeared on his face after shaving. These were hard to the touch, not tender and did not become pustular. They seemed to him to be

located under the skin. They were present for a few hours after shaving and then disappeared, to return the next time he shaved. After about two weeks they disappeared permanently. On examination a small ulcerated lesion was seen on the right tonsil and there was generalized lymphadenopathy. Results of the examination were otherwise not remarkable. A dark field examination was not made. The diagnosis was early latent syphilis.

Careful questioning of all members of the family except Clark revealed no outside contacts. Clark denied any sexual contacts for a year preceding his sore throat, but he recalled that in the winter of 1939 he had been on a "necking party" with Molly K., and a short time later had gone on a hay ride with Mary K. All other contacts were denied.

Molly K. was found to be nonsyphilitic. Mary K. could not be found. It was learned, however, that she had been admitted to the syphilis clinic of the Louisville City Hospital on Aug. 12, 1938, at which time a dark field examination of a lesion on her lower lip was positive for Spirochaeta pallida. She had received thereafter eight intravenous injections of an arsenical and eight intramuscular injections of a bismuth preparation. On September 30 she had lapsed from treatment and all efforts to trace her had been unsuccessful.

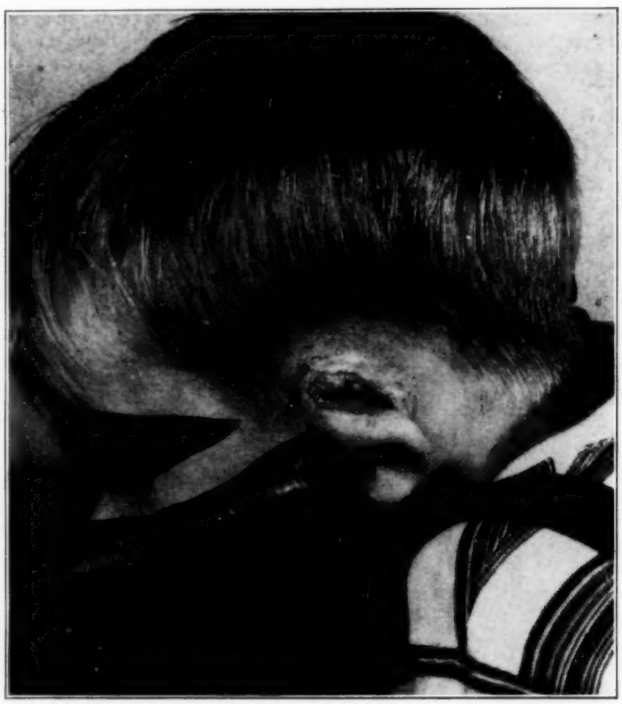

Fig. 2.—Primary lesion of syphilis behind pinna of left ear of child aged 6.

To reconstruct the history of these cases, it is reasonably certain that Mary K. was the ultimate source of these five cases of syphilis. Through kissing she transmitted the disease to Clark X, who in fondling his baby sister passed the infection to her. Jess, Valerie and Charles X were infected by the same means. It is only fortunate that the entire family was not similarly stricken, since they are affectionate people and no precautionary measures were taken.

Of great interest is the fact that two syphilitic lesions were seen by a physician and diagnoses of relatively innocuous conditions were made. It is hoped that this report will serve to lower the threshold for suspicion of syphilis in the minds of practitioners and that thorough examinations will be made of all lesions which might possibly be syphilitic.

Clinical Notes, Suggestions and New Instruments

SULFATHIAZOLE: TWO CASES OF SEPTICEMIA WITH RECOVERY

W. CALHOUN STIRLING, M.D., WASHINGTON, D. C.

The sulfonamide group of drugs has opened up tremendous potentialities in the field of chemotherapeusis and many new avenues for the use of such drugs undoubtedly will be opened.

The limitations of sulfanilamide have been realized and it has become necessary to explore the field further to find synthesized derivatives of this drug which would act where the parent drug has failed, such as in instances of Staphylococcus aureus, Streptococcus faecalis and other resistant organisms. The introduction of sulfapyridine soon followed which seemed to offer potentialities that sulfanilamide did not possess. However, it exhibited serious side effects. Antopol [1] recently reported that 40 per cent of a group of patients receiving sulfapyridine showed hematuria. Pepper and his associates found this complication in twenty-seven of 381 patients taking sulfapyridine. The formation of urinary calculi has also been reported in many instances. Nausea and vomiting not infrequently interfere with the continued administration of this drug, and it is thought to be central in type rather than due to local irritation of the stomach.

Recently two thiazole derivatives of sulfanilamide have been placed before the profession for clinical investigation. These are sulfathiazole and its methyl derivative sulfamethylthiazole. The former is the thiazole analogue of sulfapyridine: 2(para-aminobenzene sulfonamido) thiazole.

Long [2] has pointed out that the acute toxicity of sulfathiazole is definitely less than that found with sulfapyridine or sulfamethylthiazole. In experiments on rats and monkeys little evidence of injury to the body was found after these animals had been subjected to intense therapy with this drug. Van Dyke and his co-workers [3] say that sulfathiazole disappears from the blood more rapidly than does sulfapyridine and is also excreted more rapidly. The proportion of conjugated sulfathiazole excreted in the urine was also less than was the case with sulfapyridine. Long confirmed these observations, using mice for his experimental studies. For hemolytic streptococcus and pneumococcus infections in animals, sulfathiazole was found to be slightly less effective than sulfapyridine when administered by mouth. For staphylococcic infections, however, it was found superior to sulfapyridine. Further studies have shown that it is more readily absorbed from the gastrointestinal tract than is sulfapyridine and is more rapidly excreted. Less of the sulfathiazole is acetylated or conjugated in the urine than is sulfapyridine, which would therefore allow more of the free drug for bacteriostasis than would the other substances.

Hill [4] also points out that sulfathiazole is not as freely conjugated as are the other sulfamido products. White, in discussing Hill's paper, raises the question of whether sulfathiazole may undergo decomposition in the body with the excretion of a bactericidal cleavage product. Hill further states that the much larger amount of sulfathiazole which may be expected in urine as compared with sulfanilamide and sulfapyridine indicates the possibility that sulfathiazole may be a more valuable antiseptic than either sulfanilamide or sulfapyridine.

In the past, the prognosis in blood stream infections caused by the staphylococcus organism has been very poor. Kelliher [5]

Read before the Mid-Atlantic Branch, American Urological Association, Washington, D. C., April 6, 1940.

The assistance of the Department of Medical Research of the Winthrop Chemical Company made these studies possible.

1. Antopol, William: The Occurrence of Urological Complications in Humans Following Sulfapyridine Therapy, J. Urol. **43**: 589-598 (April) 1940.
2. Long, P. H.: Thiazole Derivatives of Sulfanilamide, J. A. M. A. **114**: 870-871 (March 9) 1940.
3. Van Dyke, H. B.; Greep, R. O.; Rake, Geoffrey, and McKee, Clara M.: Observations on the Toxicology of Sulfathiazole and Sulfapyridine, Proc. Soc. Exper. Biol. & Med. **42**: 410 (Nov.) 1939.
4. Hill, Justina H.: The Comparative Vitro-Action of Sulfanilamide, Sulfapyridine and Sulfathiozole in Urine, J. Urol. **43**: 491-495 (March) 1940.
5. Kelliher, T. F., and Carlen, Sidney: Treatment of Staphylococcal Septicemia with Sulfamethylthiazole: Report of a Case of Recovery, M. Ann. District of Columbia **9**: 78 (March) 1940.

recently reported a case of septicemia with recovery, sulfamethylthiazole being used as the therapeutic agent. Pool and Cook[6] report a series of cases in which sulfathiazole and sulfamethylthiazole were used and found that approximately 65 per cent of the patients were cured with this form of medication. In several of these cases the infection was caused by Staphylococus aureus and Streptococcus faecalis. They found little evidence of toxicity from either drug. Other workers, however, report that sulfamethylthiazole has produced peripheral neuritis in some instances and seems more toxic than sulfathiazole. Herrell and Brown[7] report a case of fulminating septicemia caused by Staphylococcus aureus in which sulfamethylthiazole was used with curative effects. Lindsay[8] has used both of these sulfanilamide derivatives in a number of cases of systemic infections and has found that both drugs are very effective.

REPORT OF TWO CASES

In view of the small number of similar cases reported in the literature, it is thought worth while to report two cases of septicemia in which sulfathiazole was used effectively by me.

CASE 1.—H. B., a man aged 70, entered Garfield Hospital Feb. 24, 1940, and was seen in consultation with Dr. D. W. Prentiss. The patient was in a comatose condition, which had been present for twenty-four hours. The initial attack was ushered in by a chill, rigor and marked elevation of temperature. His wife stated that he had been disoriented for the past week, gradually becoming more stuporous as the illness had progressed. He had been nauseated and vomited a greenish, bile stained fluid. During the last twenty-four hours he had had marked diarrhea. The patient had been well for the past three or four years and had never had a previous similar attack. His past history was irrelevant.

The patient was senile and completely disoriented. He was quite toxic and dehydrated, and on admission to the hospital his temperature was 101.6 F., pulse rate 140 and respiratory rate 26. His tongue was covered with a foul whitish coating. Optic and other reflexes were sluggish and the patient did not respond to questions. The chest was normal aside from evidence of a low grade hypostatic congestion of the base of both lungs. The abdomen was distended similarly to the condition seen in paralytic ileus. No masses could be palpated and no evidence of tenderness was elicited. The genitalia were normal, as was the prostate on rectal examination. Examination of the rest of the body was negative. A hemogram showed 64 per cent hemoglobin, 3,300,000 red blood cells and 12,400 leukocytes. There were 70 per cent polymorphonuclears, 7 per cent band forms, 19 per cent lymphocytes and 1 per cent monocytes. A specimen of urine showed many clumps of pus, no red blood cells and no sugar. Culture yielded Staphylococcus aureus. A moderate trace of albumin was found. A few hyaline and granular casts were seen on microscopic examination.

Nonprotein nitrogen of the blood was 75 mg. per hundred cubic centimeters. A blood culture was made by Dr. Lindsay and yielded pure Staphylococcus aureus. After a consultation, an initial dose of 4 Gm. of sulfathiazole was given, followed by 1 Gm. of the drug every six hours. This medication was continued for four days. The patient's temperature had been forming a septic curve but became normal after he was on this therapy for three days. A second culture was made after five days which yielded negative results. During the interim he was given perfusions of 5 per cent dextrose in saline solution daily to insure an adequate intake of fluids. Several days after admission to the hospital he became rational, showed interest in his surroundings and requested food. The ileus rapidly disappeared and the vomiting, which had been persistent, ceased. A third blood culture was made five days after the preceding one and was also negative.

An intravenous pyelogram was then made and showed a calculous pyonephrosis of the right kidney. The left kidney contour, pelvis and excretion were normal. Because of the anemia, he was given two blood transfusions in divided doses, which increased his red cell count to 4,350,000 and the hemoglobin content to 83 per cent.

On March 27 a right nephrectomy was carried out under spinal anesthesia and a functionless kidney was removed. Following this procedure the patient responded rapidly and is now convalescent. The sulfathiazole level of the blood was checked on alternate days during the administration of the drug and was found to average 5 mg. per hundred cubic centimeters of blood. The patient showed no evidence of toxicity until the end of the fifth day, when he became slightly nauseated and refused food. The drug was then discontinued and the nausea disappeared. His temperature has remained normal since that time.

The second case is that of a nonhemolytic streptococcus blood stream infection in which sulfathiazole quickly sterilized the blood stream.

CASE 2.—C. S. W., a man, seen on March 11, 1940, complained of severe pain over the kidney area, with nausea and vomiting. The attack was initiated by a chill followed by a sharp rise in temperature. The pain in the kidney area became more acute, requiring an opiate to relieve it. The patient had had a similar attack four weeks before while on a vacation in Florida and had been confined to his bed for two weeks. His symptoms at that time were very similar to the present ones and he was given sulfanilamide, which brought about a gradual remission of his pain and fever.

The blood culture was made by Dr. Lindsay and yielded a nonhemolytic streptococcus infection. Culture of the urine yielded the same organism, together with the colon bacillus. The hemogram showed 89 per cent hemoglobin with 8,000 leukocytes and 84 per cent neutrophils, of which 67 per cent were segmented, 15 per cent band forms, 1 per cent young forms and 1 per cent myelocytes. There were 13 per cent lymphocytes, 2 per cent large mononuclears and 1 per cent basophils. The thermal curve showed a variation of from 100.6 to 104.6 F. during the height of the attack.

The patient was placed on sulfathiazole therapy, being given an initial dose of 4 Gm., followed by 1 Gm. every six hours. Within twenty-four hours there was a marked remission of the fever and on the second day it became normal and has remained so since that time. The drug was discontinued after three days without evidence of toxicity. An intravenous pyelogram was made subsequent to this attack and showed evidence of a long standing pyelonephritis, the pelves being very small. No structural defects were noted.

ADVANTAGES OF SULFATHIAZOLE OVER SULFAPYRIDINE

Sulfathiazole seems to be less toxic than sulfapyridine, as pointed out by Herrell, Brown and others. Less of this drug is conjugated in the body, which implies a higher concentration of the drug for bacteriostasis.

Sulfathiazole is more rapidly metabolized than its predecessor. Studies of blood level concentrations and urinary excretion indicate that sulfathiazole is more quickly eliminated and that less evidence of damage to the kidneys is found. Sulfathiazole seems to possess equal bactericidal properties with sulfapyridine in staphylococcic, gonococcic, pneumococcic and meningococcic infections.

DOSAGE

Because of its rapid elimination, the interval between doses should be decreased to permit a more constant blood level concentration. In severe fulminating infections an initial dose of 2 or 4 Gm. may be given. One Gm. of the drug is then given every four hours for four or five days. Determination of the blood level concentration of the drug should be made on alternate days. Frequent urinalyses as well as checks of the red blood and leukocyte count are imperative.

Owing to the rapid absorption and excretion of sulfathiazole, the drug may be administered for longer intervals to obviate the possibility of a relapse of the infection.

CONTRAINDICATIONS TO SULFATHIAZOLE

Sulfathiazole possesses the same inherent tendency of the sulfonamide group to depress the hemopoietic system. However, this side effect has not been seen in any of my cases and can be obviated by frequent hemograms.

6. Pool, T. L., and Cook, E. N.: Sulfathiazole and Sulfamethylthiazole in the Treatment of Infections of the Urinary Tract, Proc. Staff Meet., Mayo Clin. **15**: 113-116 (Feb. 21) 1940.
7. Herrell, W. E., and Brown, A. E.: The Clinical Use of Sulfamethylthiazole in Infections Caused by Staphylococcus Aureus: Preliminary Report, Proc. Staff Meet., Mayo Clin. **14**: 753 (Nov. 29) 1939.
8. Lindsay, J. W.: Personal communication to the author, 1940.

COMMENT

I have used sulfathiazole in fifteen other cases presenting acute urinary infections, five of which were gonorrheal urethritis. In four of these cases the drug sterilized the urinary tract within five days. It is of interest to note that two of the patients had not responded to sulfanilamide therapy. The other ten patients had acute infections of the upper part of the urinary tract without evidence of obstruction. In every case the response to this form of therapy was immediate, and negative cultures were obtained in eight of the cases.

CONCLUSIONS

1. In seventeen cases of various types of urinary infections sulfathiazole was administered. Many of these patients had not responded to sulfanilamide therapy. In the two cases which are reported in detail, striking results were obtained in staphylococcic and streptococcic infections.

2. Sulfathiazole seems, in my opinion, to be less toxic and more effective than the other members of the sulfonamide group, nausea being the only side effect seen, and this quickly subsided when the drug was discontinued.

3. In staphylococcic and other sulfanilamide-resistant infections, sulfathiazole offers a new avenue of attack which in the few cases in which it has been used seems to justify the claims made for it.

4. Sulfathiazole is absorbed and eliminated more quickly than sulfapyridine, so that the concentration of the drug in the blood is more difficult to maintain at an even concentration. This difficulty is obviated by giving the drug more frequently and over a longer period of time.

NOTE.—Since this paper was written, ten other cases of infections of the urinary tract have been treated with sulfathiozole: five of prostatic obstruction, five of gonorrheal urethritis. All five of the patients with gonorrheal urethritis responded rapidly to this drug and marked improvement was noted in the others.

1621 Connecticut Avenue.

SYNDROME OF MAJOR MENSTRUAL MOLIMINA WITH HYPERMENORRHEA ALLEVIATED BY TESTOSTERONE PROPIONATE

ROBERT B. GREENBLATT, M.D., AUGUSTA, GA.

Minor menstrual molimina are accepted universally with resignation by women and as generally unworthy of consideration by the physician. Major menstrual molimina, however, may be so intense as to be manifest as unbearable premenstrual tension which endures from seven to fourteen days. The pent-up strain fortunately finds sudden release with the onset of flow. There remains, however, a group of patients who at first welcome and then dread the profuse and often protracted menstruation that follows. The tense, nerve-wrought and weary patient is further weakened by the loss of blood and finds herself cleft between Scylla and Charybdis. The syndrome of hypermenorrhea with its precursive major menstrual molimina is clear cut and distressing enough to warrant recognition and consideration. The alleviation of this syndrome by testosterone propionate therapy is frequently so striking as to merit this report.

REPORT OF CASES

CASE 1.—A white woman, aged 30, a tertipara, had been pregnant six times. The menstrual history revealed that onset occurred at 15 years of age; the cycle was irregular with intervals of two, five or seven months and was attended by severe dysmenorrhea. She had a toxemia of pregnancy in 1935. Several months after parturition the cycle regulated itself. In the past three years she presented herself at the University Hospital Outpatient Department on various occasions with premenstrual headaches, nervousness, low abdominal pain and general discomfort and at other times for dysmenorrhea and profuse menstruation. She gave a history of having had several curettages and transfusions for bouts of menorrhagia. In July 1938 curettage revealed a hyperestrogenic type of endometrium. The basal metabolism, dextrose tolerance test and blood counts were within normal limits. During the later part of 1938 she received intramuscular injections of blood from lactating amenorrheic women,[1] which more or less controlled her bouts of menorrhagia of from fifteen to twenty days' duration and reduced them to a hypermenorrhea of from seven to ten days (chart 1). Although the cycle was regular, the flow remained profuse. The prodromal syndrome of headaches, lumpy and painful breasts, abdominal bloating, nervous tension and fatigue was very marked for two weeks prior to the onset of each period. This premenstrual tension was dramatically relieved by the onset of flow.

The suction curettage performed on Feb. 2, 1939, revealed a healthy secretory endometrium. For several months attempts were made at improving the patient's general health. She received iron medication, vitamin B_1, cod liver oil, sedatives and other remedies. The syndrome of hypermenorrhea and premenstrual tension persisted. In August 1939 she received 5 and 10 mg. of testosterone propionate during the latter part of the cycle. The improvement in menstrual molimina and bleeding was remarkable. The treatment was continued each month, the doses varying from 10 to 50 mg. a month. The improvement in the tension as well as the breast pains was noteworthy and was sustained after therapy was discontinued. When estrogenic therapy was substituted, the syndrome of intense irritability and premenstrual tension returned.

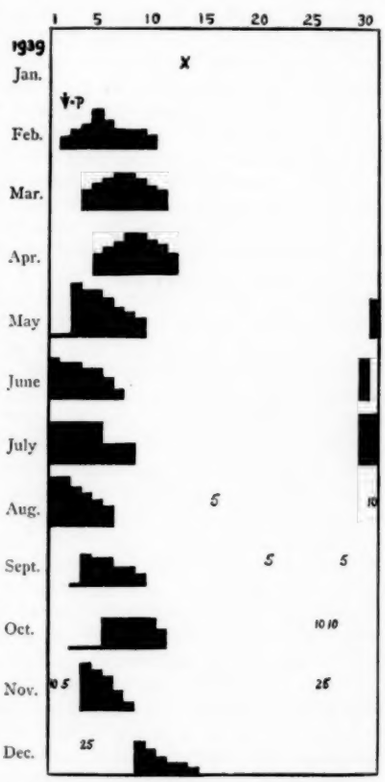

Chart 1 (case 1).—At *x* 25 cc. of blood from a lactating amenorrheic woman was administered. At the arrow suction curettage was performed, revealing an excellent progestational type of endometrium. The numerals refer to milligrams of testosterone propionate.

CASE 2.—A moderately obese white woman aged 34, a tertipara, gave a long history of hypermenorrhea. The cycle was regular, with profuse bleeding occurring for from seven to twelve days, necessitating from twelve to fifteen pads a day. Premenstrual tension, abdominal bloating, premenstrual edema, crying spells and fatigue were particularly marked in her case. Suction curettage performed in 1938 on two different occasions at the onset of menstruation revealed an excellent secretory type of endometrium. Intramuscular injections of blood from lactating amenorrheic women aided in shortening only slightly the duration of the menses but did not materially affect the profuseness of the flow. The patient could not tolerate thyroid therapy. Surprisingly enough, estrogenic therapy in very small doses improved her well-being. However, the flow was just as profuse as formerly; moreover, the premenstrual edema appeared to be more pronounced.

The administration of from 10 to 50 mg. of testosterone propionate sufficed to reduce the flow to normal (chart 2) with more or less concomitant abatement of the prodromal symptoms. The patient felt more relaxed and stronger. Abdominal bloating was greatly reduced, premenstrual edema seemed to be lessened and the patient did not weep as readily. No treatment was administered prior to her October menstrual period, and all the symptoms as well as the hypermenorrhea returned.

From the University of Georgia School of Medicine.

1. Greenblatt, R. B., and Torpin, Richard: Menometrorrhagia, J. M. A. Georgia **28**: 342 (Aug.) 1939.

However, treatment was omitted prior to her December period and the menses lasted but four days, with only two days of moderately profuse flow. The precursory symptoms seemed to be less severe than those she usually experienced prior to commencement of testosterone propionate therapy.

COMMENT

Frank [2] in 1931 reported fifteen cases of premenstrual tension and offered an acceptable explanation of the cause. Frank determined the levels of estrogen in the blood and urine of his patients and found a high renal threshold for the substance. He therefore ascribed to premenstrual tension a hormonal pathogenesis. "It would appear," he wrote, "that the continued circulation of an excessive amount of female sex hormone in the blood may, in labile persons, produce serious symptoms, some cardiovascular, but most striking definitely psychic and nervous (autonomic)." At that time he suggested temporary or permanent amenorrhea, brought on by roentgen treatment, as the proper therapeutic procedure in severe cases.

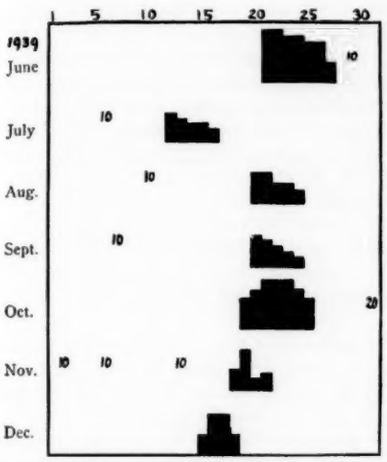

Chart 2 (case 2).—The numerals indicate milligrams of testosterone propionate. Suction curettage performed at the onset of menses on two previous occasions revealed good secretory endometrium. Note that no treatment was administered prior to the menses in October, with recurrence of the syndrome.

Israel [3] contested the explanation offered by Frank and suggested that premenstrual tension is caused not by an excess of circulatory estrogen but rather by the presence of unantagonized estrogen. By this he implied that the primary cause of premenstrual tension is deficient ovarian luteinization with a decreased production of progestin. He therefore suggested progesterone therapy and/or low dose irradiation of the pituitary gland and ovaries. Among my records I found one report of a patient with marked premenstrual tension and dysmenorrhea who bled at irregular and lengthened intervals from a hyperestrogenic endometrium. Cyclic administration of progesterone regulated her cycle and gave her complete relief.

The excellent progestational endometrium obtained at the onset of menstruation in my cases of cyclic hypermenorrhea with prodromal manifestations of major menstrual molimina precludes the complete acceptance of a hypothesis of corpus luteum deficiency. In another patient with this syndrome urinary pregnandiol glucuronide estimations were normal while urinary estrogens were insufficient for assay. I have noted among patients with varied degrees of menstrual molimina that estrogenic therapy frequently aggravated the prodromal symptoms and that when small doses of testosterone propionate were substituted the patient felt more relaxed. The employment of male sex hormone in the treatment of certain gynecic disorders [4] may appear paradoxical but is not unphysiologic. Womack and Koch [5] reported that normal women excreted quantities of androgens comparable to those excreted by normal males. The Callows [6] isolated from the urine of normal women the same two androgens identified in the urine of normal males by Butenandt and his co-workers. The administration of chemically pure androgenic substances to relieve the syndrome of major menstrual molimina with hypermenorrhea seems indicated whether one accepts the explanation of hyperestrogenemia (Frank) or the concept of unantagonized estrogens (Israel). The indication finds further support in that male sex hormone nullifies and neutralizes the action of estrogens, for Shorr, Papanicolaou and Stimmel [7] found that the follicular smear obtained with the injection of estradiol benzoate could be abolished by simultaneous injection of testosterone propionate.

CONCLUSION

The syndrome of major menstrual molimina associated with excessive cyclic bleeding is most harassing and distressing. Small doses of testosterone propionate were administered to two patients presenting such a syndrome with sufficiently good results to warrant its further trial.

2. Frank, R. T.: The Hormonal Causes of Premenstrual Tension, Arch. Neurol. & Psychiat. **26:** 1053 (Nov.) 1931.
3. Israel, S. L.: Premenstrual Tension, J. A. M. A. **110:** 1721 (May 21) 1938.
4. Salmon, U. J.; Geist, S. H., and Walter, R. I.: Treatment of Dysmenorrhea with Testosterone Propionate, Am. J. Obst. & Gynec. **38:** 264 (Aug.) 1939. Geist, S. H.; Salmon, U. J., and Gaines, J. A.: The Use of Testosterone Propionate in Functional Bleeding, Endocrinology **23:** 784 (Dec.) 1938. Varangot, J.: L'action de la testosterone et de ses esters sur le tractus génital des femelles de mammifères et de la femme, Ann. d'endocrinol. **1:** 55 (March) 1939.
5. Womack, E. B., and Koch, F. C.: Testicular Hormone Content of Human Urine, Endocrinology **16:** 273 (May-June) 1932.
6. Callow, Nancy H., and Callow, Robert K.: Isolation of Androsterone and Transdehydro-Androsterone from Urine of Normal Women, Biochem. J. **32:** 1759 (Oct.) 1938.
7. Shorr, Ephraim; Papanicolaou, G. N., and Stimmel, B. F.: Neutralization of Ovarian Follicular Hormone in Women by Simultaneous Administration of Male Sex Hormone, Proc. Soc. Exper. Biol. & Med. **38:** 759 (June) 1938.

A CONVENIENT METHOD OF APPLYING WET DRESSINGS

GAROLD V. STRYKER, M.D., AND JOSEPH GRINDON JR., M.D.
ST. LOUIS

Various dermatoses affecting the hands and feet require the application of continuous wet dressings. The manner of application and the means of maintaining the moisture of such dressings present a practical problem. Sheets of wet proof material consume time to apply properly, are difficult to keep in place and are necessarily bulky.

Fig. 1.—Pliofilm mitt.

These difficulties are overcome by the use of mitts and socks made of pliofilm.[1] This material is moisture proof, oil proof, odorless, nonirritating, pliable, thin, durable, tear resistant, sewable, heat sealing, not uncomfortably warm, noninflammable, resistant to weak acid and alkali and inexpensive.

From the Department of Dermatology, St. Louis University School of Medicine.

1. Pliofilm is made by the Goodyear Tire & Rubber Company, Inc.

Previously, one of us had employed rubber gloves and socks to maintain wet dressings over night. These were therapeutically effective, though patients objected because of constriction and excess heat.

Mitts and socks made of pliofilm have now been in use over a period of nine months, a total of eighty-seven private patients having been so treated. In no case was there any evidence of irritation or serious complaint from the patient. In many instances the patient is grateful for the symptomatic relief obtained by the wet pack. By this method it has been possible to use continuous wet packs in cases in which before, owing to the inconvenience of application experienced, it would not have been feasible. In order to insure comfort, the coverings should be large enough to cover the dressings and at the same time permit some movement of the fingers and toes. To prevent drying, the pliofilm must come in contact with the skin of the wrist or ankle above the dressing.

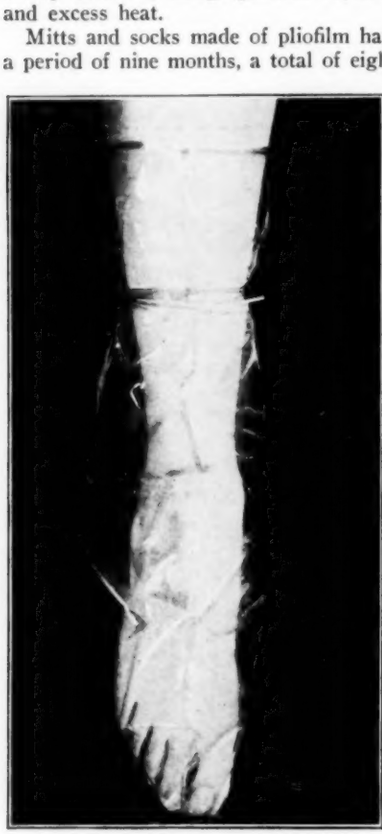

Fig. 2.—Pliofilm sock.

In subacute and chronic phytosis of the hands and feet, boric acid solution packs with pliofilm mitts and socks are used at night and a suitable antifungicidal ointment is applied during the day.

634 North Grand Avenue.

A MICRO BEDSIDE TEST FOR THE DETERMINATION OF THE SULFANILAMIDO GROUP CONCENTRATION IN BODY FLUIDS

E. W. Schoeffel, Ph.D., Chicago

The widespread therapeutic use of drugs containing the sulfanilamido grouping is safeguarded by methods which permit the constant observation of the effective concentration in the body fluids. However, the many untoward effects produced by these drugs force the physician to keep a close watch over his patients because of individual differences in toleration. (For toxic manifestations the blood picture is of major importance.) In the main, Marshall's [1] method is used. Several modifications of this test have recently been reported [2] which aim to simplify existing clinical laboratory procedures.[2]

All known modifications were compared with one another. The following procedure was found to be simple, brief, feasible and economical. The method is reliable and reproducible in the hands of student technicians. Since it is not necessary to report levels at all times in minute fractions but distinctions must be made between such concentrations as 3.5 and 4 or 2.5 and 3 mg. per hundred cubic centimeters of body fluids, this new modification is considered to rank with present procedures. Marshall's method together with the spot test filter paper method form the principal means by which this rapid test is accomplished. It is fitted for determination of the drug concentration in the blood, without the aid of laboratory facilities, by the physician or his technician at the bedside even in rural districts.

Drs. W. C. Beck and H. J. Yellen, Cook County Hospital, gave permission to use samples of blood and of urine, and Dr. Howard Glass of the pharmacologic department of the University of Chicago compared the results of the Marshall procedure with those of the micro bedside method.

1. Bratton, A. C., and Marshall, E. K., Jr.: New Coupling Component for Sulfanilamide Determination, J. Biol. Chem. **128:** 537-550 (May) 1939.

2. Ratish, H. D., and Bullowa, J. G. M.: A Bedside Test for Sulfapyridine, J. Lab. & Clin. Med. **25:** 655 (March) 1940. Chinn, Herman, and Bellows, John: The Distribution of Sulfapyridine in the Body, ibid. **25:** 735 (April) 1940. Demonstration before Cook County Hospital; personal communication to the author by the Chicago Branch Laboratory of the Illinois Department of Public Health. Vasterling, P.: The Influence of Sulfanilamido Derivatives on Urine Analysis, Deutsche Apotheker-Zeitung **55:** 213 (April 6) 1940. James, G. V.: The Determination of Members of the Sulfanilamide Group of Drugs, Analyst **65:** 206 (April) 1940.

PROCEDURE FOR THE DETERMINATION OF THE SULFANILAMIDO DERIVATIVES BY THE MARSHALL SPOT TEST, FILTER PAPER METHOD

A. Place a drop of the body fluid under examination (approximately from 0.01 to 0.05 cc.) with calibrated pipets of the blood pipet type in the depression of a hanging drop slide. (The liquid may be dried by air current. If the material must be shipped, the dried substance is covered with a drop [from 0.050 to 0.075 cc.] of liquid petrolatum U. S. P. and the cover slip fastened on with a seal.) Place all slides on a clean white towel.

B. Add 0.02 cc. of four normal hydrochloric acid and 0.02 cc. of 10 per cent trichloroacetic acid to the material in the depression. Break up and stir thoroughly with a glass thread. For total sulfanilamide heat over an alcohol lamp to near dryness and repeat step B.

C. Add 0.03 cc. of 0.1 per cent sodium nitrite solution and stir the mixture thoroughly for thirty seconds (with amounts of free sulfanilamide in excess of 20 mg. for 100 cc. use 0.05 cc.) with a glass rod.

D. Add 0.02 cc. of a solution containing 0.1 per cent ammonium sulfamate and stir the solution thoroughly (for larger amounts of sodium nitrite use corresponding amounts of the sulfamate solution).

E. Add 0.02 cc. of 0.4 per cent aqueous solution of N(1-naphthyl)-ethylenediamine dihydrochloride (Marshall's reagent; the solution should be kept in a dark brown bottle and only enough made up to last two days). Stir the mixture thoroughly.

F. Prepare standards (as described under standard reagents and apparatus to be used for the test) containing 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12.5 and 15 mg. per hundred cubic centimeters. If testing for sulfanilamide, use sulfanilamide in the standards; if testing for sulfapyridine or sulfathiazole, use sulfapyridine or sulfathiazole standards, respectively. Such standards are good for one week if kept in an ice box and away from direct light. The standards may be conveniently prepared by carefully diluting a larger amount.

G. Insert in the depression containing the now red solution a strip of filter paper and let the liquid spread by capillary action over one end of the paper (precipitated protein material does not interfere with the test). Compare the unknown samples with the standards. The developed color depends on the drug used. (It is therefore necessary for the technician to know which of the sulfanilamido derivatives were used. It is important to know whether other therapeutic agents were also used. Especially with specimens of urine a slight color variation may be noticed, depending on various diazotizable substances. Since no fractions are to be determined and only round figures given [2.5, 4 and 7.5 mg. per hundred cubic centimeters], no strong interference exists.) The color on the filter paper will slowly fade but will hold distinctive and discernible hues for a period of days when compared with standards prepared on the same day and kept under the same conditions. Actual color charts may also be prepared to facilitate the determination at the bedside. In general for ease of reproduction the final amount of liquid in the depression should not exceed the approximate amounts of from 0.125 to 0.150 cc.

STANDARD REAGENTS AND APPARATUS TO BE USED FOR THE TEST

1. Standards containing drugs of the various sulfanilamido groupings in progressive proportions from 0.5 to 15 mg. per hundred cubic centimeters of liquid, depending on the accuracy desired. Amounts of 2.5, 5, 7.5, 10 and 15 mg. per hundred cubic centimeters are sufficient for reporting the concentration in body fluids. (The standard solutions should be made up to a p_H of 5 with trichloroacetic acid solution.)

2. Hydrochloric acid, four normal.[3]
3. Trichloroacetic acid, 10 per cent solution.
4. Sodium nitrite, 0.1 per cent solution.
5. Ammonium sulfamate, 0.1 per cent solution (containing 0.1 Gm. ammonium sulfamate per hundred cubic centimeters of distilled water).[3]
6. Marshall's reagent, 0.4 per cent strength (containing 0.4 Gm. of N(1-naphthyl) ethylenediamine dihydrochloride in 100 cc. of distilled water).
7. Filter paper (absorption strip paper for spot testing).[4]
8. Hanging drop slides, cover slips and sealing material.
9. Liquid petrolatum U. S. P.
10. Glass threads.
11. Suitable pipets (blood pipets or any other pipets standardized to require volume relationship).
12. Equipment for obtaining blood from the finger or ear or for drawing spinal fluid.
13. Alcohol lamp.

535 North Dearborn Street.

MYASTHENIA GRAVIS: TREATMENT BY IMPLANTATION OF DESOXYCORTICOSTERONE ACETATE PELLETS

ROBERT C. MOEHLIG, M.D., DETROIT

The more recent development of endocrine chemistry with the manufacture of synthetic, relatively insoluble, products bids fair to become an excellent way of treating chronic endocrine deficiencies. The advantages of this form of treatment are many and obvious.

I have recently treated a patient with a severe fulminating form of myasthenia gravis by the subcutaneous implantation of desoxycorticosterone acetate pellets.

REPORT OF CASE

M. G., a physician aged 32, complained Oct. 6, 1939, of severe dyspnea and rapid fatigability. The following is a report of his illness as written out by himself:

"The onset of the disease was insidious but rapid. There were no prodromal signs or symptoms of any infectious process.

"Dyspnea with the slightest exertion and fatigability with weakness were the major complaints. These were rapidly progressive over a period of seven days to the point of orthopnea and prostrating fatigue with but small effort. The patient could hardly raise his arms to shave or comb his hair.

"The weight of the head and shoulders and the effort to hold himself upright seemed intolerable and impossible. The muscles of the face, neck, shoulders, arms and chest were more involved than those of the abdomen and the lower extremities. The abdomen, however, became lax and protuberant, and defecation became more difficult.

"Impairment in swallowing foods or liquids progressed to inability to eat. Air was swallowed with all eating and drinking, producing excessive belching and gas pains.

"Paresis of the pharyngeal and laryngeal muscles produced a nasal, higher pitched voice, and talking was a decided effort, requiring frequent intervals of rest to avoid development of a whisper.

"Anorexia became complete in one week. All foods tasted alike. There was an 8.2 Kg. (18 pounds) weight loss within two weeks.

"The hard palate and nasopharynx were felt to be uncomfortably dry at all times.

"When the first symptoms of dyspnea and fatigue on exertion were noted, a generalized cold sweat would result from continued effort to be up and about . . . this, however, quickly changed to a dry skin with no sweating regardless of the amount of exertion.

"Orthopnea lasted for several nights and the weight of his arm on his chest wall could not be tolerated. The patient describes his dyspnea rather as an 'air hunger.' It was obvious to him that chest expansion and diaphragmatic excursion were diminished.

"Exertion always produced a bothersome tachycardia and palpitation, although no irregularity was noted.

"The patient had always been active and rarely took a nap or daily rest period. Shortly after onset, however, he felt utterly exhausted most of the time and was quite drowsy. He could readily fall asleep in a chair at any time of the day. Frequent short rest periods enabled him to continue with his work after treatment was started, although he never felt rested or strong, regardless of the sleep or rest he obtained.

"Sexual desire and powers were not affected. The sphincters were also normal."

The patient was tall and slender: 186.7 cm. (73½ inches) in height and 72.6 Kg. (170 pounds) in weight. He gave the appearance of being very ill.

He was extremely tired and exhausted. The expression of his face was apathetic and sad. The upper eyelids were ptotic and the forehead was wrinkled. Talking was obviously a great effort. He was able to say but a few words at a time and then had to wait a few minutes before resuming. He was incapable of any sustained muscular effort such as holding out his arms. His leg muscles tired easily when the leg was stretched out. Dyspnea was very obvious, and his respirations were about 30 a minute.

He had hyperextensibility of the joints, such as of the phalangeal and elbow joints.

The skin and mucous membrane of the mouth and of the pharynx were very dry. As he said, no matter how often he moistened his mouth with fluids his mouth would remain dry. Previously he had perspired profusely, especially in the axilla.

There was a tendency to external strabismus of the right eye. Nystagmus was not present. He had a high arched palate. The thyroid gland was palpable but not nodular. The heart and lung sounds were normal. There were no pathologic reflexes. Pes planus was present. The blood pressure was 110 systolic, 62 diastolic.

The serious condition of the patient called for immediate treatment, and urinary creatinine and other studies were not made.

The patient had three operations on his right eye for strabismus early in life. He had the usual childhood diseases.

The father is living and is a large, heavy set, muscular person, height 185 cm. (73 inches), weight 99.8 Kg. (220 pounds). The mother is living and is a heavy set woman, height 177.8 cm. (70 inches), weight 86.2 Kg. (190 pounds). A paternal uncle and a paternal aunt died of pulmonary tuberculosis. They were tall and slender. The patient is married and has one child.

October 7, treatment was begun as follows:

Quinine 0.6 Gm. three times a day, aminoacetic acid 4 Gm. three times a day and desoxycorticosterone acetate 5 mg. a day subcutaneously was the regimen. The quinine was discontinued after a few doses because of unpleasant effects.

As the first week passed under this therapy the patient's condition seemed to be about stationary. He was able to be up and about with difficulty. The aminoacetic acid was stopped after a few days. During the second week the injections of desoxycorticosterone acetate were increased to 10 mg. a day and definite, immediate alleviation of the fatigue and weakness was noted. This invariably occurred from five to six hours after the injection. The patient continued to improve slowly over the next ten days.

The daily injection of 10 mg. of desoxycorticosterone acetate was continued until October 28, when three pellets of 150 mg. each, or 450 mg., were implanted in the subcutaneous tissue of the left side of the abdomen.

Injections of the desoxycorticosterone acetate were stopped two days after the operative procedure. The patient's condition remained unchanged until the fifth day after the implantation, when he again rather suddenly noted another more marked alleviation of his symptoms.

Since then improvement has been gradual but steady, until at present, three and a half months after implantation of the pellets, no symptoms of the disease are noticeable. All loss of weight has been quickly regained.

As regards treatment, the patient's observation was that the quinine was of no apparent value. The aminoacetic acid was of very questionable value. The injections of desoxycorti-

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3. This may be omitted when rough approximations are being made.
4. This filter paper was obtained from Sargent & Co., Laboratory Supply House, Chicago.

Dr. Max Gilbert, of the Schering Corporation, supplied the desoxycorticosterone acetate material used.

From the Department of Internal Medicine, Harper Hospital and Wayne University College of Medicine.

costerone acetate were of definite though but temporary benefit, while the effect of the pellet implantations has been close to miraculous in its sustained and complete relief of symptoms.

Laboratory studies made Jan. 29, 1940, were as follows: blood sugar 70 mg., blood cholesterol 191 mg., nonprotein nitrogen 37.5 mg., blood creatinine 0.65 mg. (normal 1 to 2 mg. per hundred cubic centimeters of blood), urinary creatinine 13 mg. in twenty-four hour specimen of urine (normal 1 to 1.25 Gm. per twenty-four hour specimen) and blood chlorides 300 mg. of total chlorides as sodium chloride per hundred cubic centimeters of blood (normal from 570 to 620 mg. in 100 cc. of plasma).

It is unfortunate that comparative studies could not be made at the time the condition was at a crisis. It is of interest that the plasma chloride and blood sugar are lower than normal and are similar to the values seen in Addison's disease. This also holds for the nitrogen, which is somewhat higher than normal. Whether this means that the muscle was utilizing the creatinine after therapy rather than excreting it, as is usual in myasthenia gravis, is of course conjectural.

COMMENT

The diagnosis of myasthenia gravis was made on the basis of the history and objective manifestations. This was a very fulminating and severe type of the disease. The loss of weight was rapid owing to the patient's inability to eat properly, since solid foods would produce choking. The dyspnea was very marked, as was the muscular fatigue. His appearance was alarming.

The relief obtained by the injections of desoxycorticosterone acetate was definite and was more marked as the dosage was increased to 10 mg. a day. However, the most dramatic and striking improvement followed the implantation of the desoxycorticosterone acetate pellets. His improvement continued until February 20, 115 days after implantation, without a sign of recurrence and as late as June 7 he was still in good condition. He carries on his routine duties as a physician and is also able to carry on other activities such as dancing. He has regained the loss of weight so that he now weighs 80.7 Kg. (178 pounds). The dryness of the skin has also disappeared.

The rationale leading to the use of this synthetic adrenal cortical derivative was based on several factors. In a general way asthenia is an outstanding symptom of both Addison's disease and myasthenia gravis, although in the latter disease the fatigability comes only when the involved muscles are called on for sustained effort.

It was noted in the patient's past history that he had suffered from strabismus in infancy. This would indicate muscular weakness and, in view of the subsequent history, a congenital predisposition to muscle metabolism disturbance.

Both pituitary and adrenal cortex glands are concerned with muscle metabolism.

Houssay,[1] in his article on asthenia hypophysopriva, shows experimentally that the neuromuscular symptoms are due to alterations in the pituitary. He said "A neuromuscular syndrome appears in the hypophysectomized amphibians some weeks after operation and gradually becomes worse, terminating in death. Hypophysectomized toads (or toads from which the principal lobe has been removed) always become asthenic or adynamic at a later stage. Death occurs three to thirty days after the appearance of the asthenia, most of the toads dying between four and seven weeks after operation."

Pituitary insufficiency such as pituitary cachexia produces a very marked muscular asthenia comparable to that seen in Addison's disease.[2]

Houssay[1] found that the phosphocreatine (and also the total phosphorus) of the muscles was lowered after hypophysectomy. The muscular and hepatic glutathione diminishes. The resting muscular lactic acid is normal, but it increases less during tetanus than in the control patients.

In myasthenia gravis the excretion of creatinine is increased.

Houssay said "Adrenal insufficiency, which occurs frequently in cases of pituitary insufficiency, probably increases the asthenia but it is not certain, nor even likely, that the asthenia has an exclusively adrenal origin." Adrenal cortex extract "does not correct asthenia hypophysopriva as does the anterior pituitary extract. It is more probable that there is a direct metabolic action of the pituitary hormone. On the other hand the actions of the adrenals and pituitary on the carbohydrate metabolism have a certain similarity (the glycogenetic action, etc.) and anterior pituitary extract has a diabetogenic activity in adrenalectomized toads. Pituitary asthenia, therefore, appears to be due to general nutritive changes which principally affect the function of the central nervous system."

From the foregoing, a pituitary etiology of this condition seems not unlikely. If this is true, how does the synthetic adrenal cortical hormone produce its benefits? Probably by a secondary effect on the pituitary. Bates and I[2] showed that in an adrenal hypernephroma associated with polycythemia pituitary basophilism may be present. Furthermore primary adrenal cortex tumors which give a clinical picture simulating Cushing's pituitary basophilism no doubt activate the pituitary even though a basophil adenoma is not present.

I have seen a few cases of pituitary dystrophy associated with progressive muscular atrophy and these patients, I believe, have a definite pituitary disturbance which is responsible for the muscular disease. Certainly the experimental work of Houssay would tend to strengthen this idea.

I have touched on some of these points in other articles, such as on the pituitary and adrenal cortex.[3]

It was noted by the patient that soon after the onset of the disease the skin became dry and there was no sweating, regardless of the amount of exertion. This is a symptom of pituitary insufficiency as emphasized by Houssay[1] and shown experimentally by his pupil Aubrun.[4] Hypophysectomy in the toad produced cutaneous hyperkeratinization because of an exaggerated production and a failure of normal desquamation of the horny layers. The marked diminution of cutaneous secretions appears within from fifteen to twenty-five days after hypophysectomy. Injection of anterior pituitary extract restores the secretion of the skin.[4]

An inherited congenital muscular weakness in a person who is the offspring of hyperpituitary parents seems to me to be quite a logical hypothesis as the etiologic factor of myasthenia gravis; why, if this is correct, would the patient show what represents a hypopituitary disturbance?

It will be noted that a paternal uncle and aunt were asthenic and died of pulmonary tuberculosis. It is a well known fact that asthenic persons have, among other mesodermal weaknesses, poorly developed muscles and supportive structures.

Did this muscular weakness manifest itself congenitally in the patient as poorly developed musculature, as shown by the strabismus, hyperextensibility of the joints and pes planus?

Did this gland, when the patient reached the age of 32, produce a metabolic disorder in a congenitally weakened muscular system that manifested itself clinically as myasthenia gravis?

Schlezinger[5] concluded from the results of therapy in seven cases of myasthenia gravis that anterior pituitary extract and aminoacetic acid are ineffective remedies. He found that the most satisfactory form of therapy in the absence of toxic manifestations consists in the oral administration of combined prostigmine and ephedrine medication.

Simon[6] treated two cases of myasthenia gravis with anterior pituitary extract; the symptoms subsided with this form of therapy.

That the latter is a doubtful remedy, even if there is an involvement of the pituitary, is shown by the fact that solution of anterior pituitary in the form of "antuitrin" is not standardized and is of very questionable potency.

Prostigmine, as Schlezinger says, causes no permanent cure; "as with insulin in diabetes, continued administration is required. Progression of the disease may result in death despite the use

1. Houssay, B. A.: Functions of the Pituitary Gland, New England J. Med. **214:** 913-926 (May 7), 961-971, 971-986 (May 14), 1023-1030 (May 21), 1086-1092 (May 28), 1128-1136, 1137-1146 (June 4) 1936.

2. Moehlig, R. C., and Bates, G. S.: Influence of the Pituitary Gland on Erythrocyte Formation, Arch. Int. Med. **51:** 207-236 (Feb.) 1933.

3. Moehlig, R. C.: Pituitary Gland and Suprarenal Cortex, Arch. Int. Med. **44:** 339-343 (Sept.) 1929; Selective Action of Suprarenal Cortex Secretion on Mesothelial Tissues, Am. J. M. Sc. **168:** 553-564 (Oct.) 1924.

4. Aubrun, E. A.: Sintomas cutáneos de los sapos hipofisoprivas, Rev. Soc. argent. de biol. **11:** 371-380 (Sept.) 1935; Symptomes cutanés du crapaud hypophysoprive, Compt. rend. Soc. de biol. (Buenos Aires) **120:** 734, 1935.

5. Schlezinger, N. S.: Evaluation of Therapy in Myasthenia Gravis, Arch. Int. Med. **65:** 60-77 (Jan.) 1940.

6. Simon, H. E.: Myasthenia Gravis, J. A. M. A. **104:** 2065 (June 8) 1935.

of prostigmine. Certainly implantation of pellets of desoxycorticosterone acetate, if the remedy is efficacious, is a much more satisfactory mode of therapy.

Thorn and his associates[7] found that the daily absorption of the pellets ranged from 0.25 to 0.3 mg. a day. Therefore on the basis of 0.3 mg. per pellet a day, roughly 1 mg. for the three pellets, the implanted supply would last approximately 450 days.

SUMMARY

Myasthenia gravis of the fulminating type with rapid loss of weight due to pharyngeal muscle weakness, dyspnea and muscular asthenia occurred in a physician aged 32; he was treated by hypodermic injections of synthetic adrenal cortical hormone (desoxycorticosterone acetate) and by implantation of three pellets (150 mg. each) into the subcutaneous tissue of the abdomen.

A pituitary etiology with a congenital inherited defect of the muscular system is postulated.

Improvement following the use of desoxycorticosterone acetate was both striking and dramatic.

While it is appreciated that remissions may and do occur in this disease, the patient's condition was precarious and the disease was rapidly progressive, so much so that death from respiratory muscular paralysis seemed imminent.

Naturally, further experiences with other patients as well as the continued progress of this patient is desirable before final conclusions concerning lasting benefits are made.

964 Fisher Building.

AN UNUSUAL CASE OF DUODENAL FOREIGN BODY

T. P. BROWN, M.D., AND ROBERT S. CREW, M.D.
PHILADELPHIA

E. W., a Negro woman aged 69, was admitted to the medical service of Dr. Russell S. Boles at the Philadelphia General Hospital, Aug. 15, 1939. Her chief complaint at that time was pain in the upper part of the abdomen. She had apparently been well until August 8, when she noticed a persistent dull pain in the right upper quadrant. She had been nauseated but had not vomited; the bowels had been regular; she had not observed any bloody, tarry or clay colored stools; her weight had been stationary.

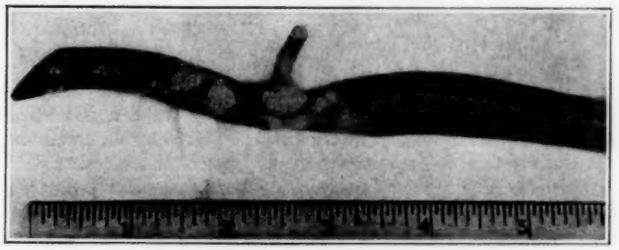
Except for a cholecystectomy in 1931, her past medical and her family history were essentially negative. In 1933 and again in 1936 she had attacks of colicky pain in the right upper quadrant, which subsided promptly following medical treatment.

Physical examination showed no apparent abnormalities except an upper right rectus scar and a large firm irregular mass extending across the right upper quadrant of the abdomen, apparently attached to the liver. It was slightly tender on deep pressure and moved with respiration. At the time of examination a tentative diagnosis of metastatic carcinoma of the liver was made.

Laboratory studies showed nothing significant: The red blood cell count was 3,220,000, the hemoglobin content was 75 per cent, the white cell count was 12,000 and the differential count was normal. The blood urea nitrogen was 9 mg. per hundred cubic centimeters; blood sugar was 68 mg. The Wassermann reaction of the blood was negative. Gastric analysis showed an absence of free hydrochloric acid, low total acidity and an absence of lactic acid and occult blood.

August 17, a flat x-ray film of the abdomen was made and revealed that there was a drainage tube about 17 cm. long just to the right of the spine; the kidneys were well visualized and normal in size and position. The psoas line on the left was well outlined but on the right was obscured.

August 24, under cyclopropane and ether anesthesia, a laparotomy was performed by Dr. P. A. McCarthy. When the peritoneum was opened the mass described was found to be omentum which was wrapped around the lower edge of the liver and was adherent to the gallbladder fossa. The gallbladder was absent and the common duct was slightly dilated and tortuous. The tube reported by the roentgenologist was felt through the wall of the duodenum. The latter was opened and a large twisted horizontal bar of a T tube was removed. The vertical, or drainage, bar had been broken off and the part retained had migrated into the duodenum, where further migration had been interrupted by the angulation of the duodenojejunal junction. The duodenum was closed, the upper part of the abdomen explored and the abdominal wall closed. Convalescence was uneventful except for a stitch abscess. The patient was discharged symptom free September 13.



Horizontal section of T drainage tube which had been inserted into the common bile duct and was found eight years later in the duodenum.

Her previous record showed that she had had a cholecystectomy performed in 1931 and had been discharged with a T tube in situ. At that time she was instructed to return to the surgical clinic for after-care but failed to do so and did not obtain other professional treatment.

COMMENT

This case is of interest in that (1) it illustrates that a sizable foreign body can remain in the duodenum for a long period without producing notable symptoms, (2) it shows that a relatively large foreign body placed in the common duct can migrate to the duodenum, and (3) it reemphasizes the necessity of strict follow-up supervision in this type of case.

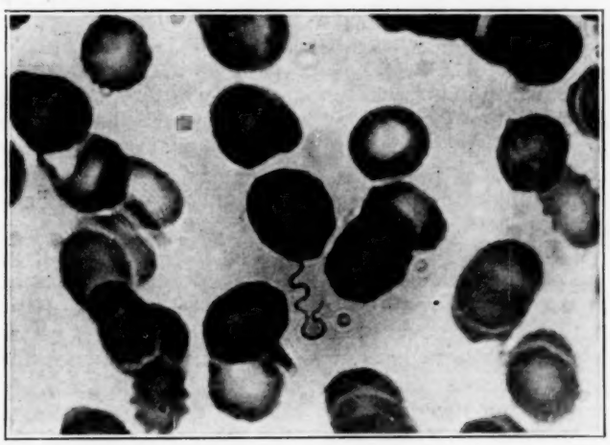
Philadelphia General Hospital.

REPORT OF A CASE OF RELAPSING FEVER

W. P. NEILSON, M.D., ENID, OKLA.

Relapsing fever, a disease found with relative frequency in certain tropical countries, has been rarely observed in the United States. For this reason, a typical case observed in a Midwestern state is of interest.

A woman aged 40 when seen on Dec. 19, 1939, had been ill for about six weeks. Her illness was characterized by recurrent attacks of elevations of temperature and repeated chills. She had been under medical treatment throughout this time, having been treated symptomatically, chiefly with large doses of quinine. There had been no improvement.



Blood smear highly magnified.

On routine examination I found that agglutination tests with antigens from tularemia, typhoid and undulant fever were all

7. Thorn, George; Howard, R. P.; Emerson, Kendall, Jr., and Firor, W. M.: Treatment of Addison's Disease with Pellets of Crystalline Adrenal Cortical Hormone (Synthetic Desoxycorticosterone Acetate) Implanted Subcutaneously, Bull. Johns Hopkins Hosp. **64**: 339-366 (May) 1939.

negative. There were no abnormal urinary changes. All physical examinations were negative. When I examined the blood smears I found many spiral organisms present. These spirochetes were unusually long, with seven or eight spirals. They were attached to the border of the red cells and extended well down into the intercellular spaces. I made a diagnosis of relapsing fever, although I had not previously seen a case. The laboratory examinations and the clinical picture made such a composite whole that I felt that the diagnosis was obvious.

On admission, the patient's temperature was 105.5 F. At 3 p. m. I gave her 0.4 Gm. of neoarsphenamine. At midnight her temperature was normal. Since that date there has been no further elevation. This is not surprising when it is realized that in the treatment of these cases in tropical countries one dose of 0.3 Gm. is curative in 80 per cent of the cases.

This case was reported to the Oklahoma State Health Department, with an inquiry about previous cases in the state. I was informed that no previous case has ever been reported in the state.

I am at a loss to know the origin of this infection; however, these facts are pertinent:

1. The patient has not been away from her immediate vicinity.
2. No foreign guest has visited the home.
3. There is no history of an insect bite or any other external lesion.
4. The patient lives on a farm in the wheat plains area; rodents are very few. She does no outside farm work.
5. I have been unable to find any more cases in this community.

The accompanying photomicrograph was made by the laboratories of the Oklahoma University Medical School.

502 West Randolph Street.

Special Article

CONFERENCES ON THERAPY

THE TREATMENT OF BLOOD DISORDERS

VII. LEUKEMIA, AGRANULOCYTOSIS AND NEUTROPENIA

NOTE.—*These are actual reports, slightly edited, of conferences by the members of the Department of Pharmacology and of Medicine of Cornell University Medical College and the New York Hospital with the collaboration of other departments. The questions and discussions involve participation by members of the staff of the college and hospital, students and visitors. The next report will concern "Treatment of Blood Disorders: VIII. Hemorrhagic Diseases."*

DR. JACOB FURTH: Leukemia and agranulocytosis or neutropenia are two fundamentally different diseases, although the terminology would suggest that one is merely a depression, the other a stimulation, of leukopoietic activity.

Agranulocytosis or a milder form of it, neutropenia, can be produced by a variety of agents, and the process is reversible; that is, when the causative agent is removed complete restitution may occur. Leukemia, on the contrary, is a neoplastic disease of leukopoietic tissues, and removal of the causative agent after establishment of a neoplasm will no longer influence the course of the disease. This fundamental concept emphasizing the difference between these two types of disturbance is essential to the understanding of the established treatment of these diseases and to the evaluation of the new procedures that are proposed periodically.

In agranulocytosis, necropsy reveals either a hypoplasia of the granulocytic elements of the bone marrow or a normal number and occasionally an increased number of myeloblasts with failure of maturation. It is assumed that at first maturation of the myeloblasts is arrested; and this is followed by an atrophy of the granulocytic elements of the bone marrow. We know of no agent that arrests maturation without producing subsequently a hypoplasia of the bone marrow. A maturation factor analogous to that influencing erythropoietic activity has thus far not been demonstrated in relation to the leukopoietic systems.

There are many agents which depress the granulocyte-forming elements of the bone marrow. These are: (*a*) chemicals, such as arsphenamine, benzene and related compounds, aminopyrine, dinitrophenol and more recently sulfanilamide and allied substances; (*b*) bacterial and protozoan products, e. g. those observed with streptococcic infections or kala-azar; (*c*) physical agents, as x-rays. Some of these agents act in almost every individual exposed, while others act only in a few of the individuals so exposed, who are assumed to be hypersusceptible to the specific agent. Cases in which the cause of agranulocytosis is not evident are spoken of as idiopathic, but there is no reason to believe that these forms of agranulocytosis differ in any way from those that are produced by known agents.

Leukocytes are constantly needed to ward off infections from micro-organisms that are normal inhabitants of mucous membranes. The chief danger in agranulocytosis is the absence of this normal protecting mechanism. Bacteria invade the mucous membranes, producing a necrotizing inflammation. Necrotizing angina can be both the result and the cause of agranulocytosis. In the *Index Medicus* agranulocytosis is listed only under "angina, agranulocytic." However, similar necrotizing inflammation with agranulocytosis may occur in places other than the oral cavity; it is not uncommon in the gastrointestinal tract. The goal of treatment is first to discover and remove the causative agent and then to stimulate granulocyte formation and maturation.

Leukemia is a neoplastic disease in which the malignant cells are primitive blood cells capable of unrestrained multiplication. The evidence in favor of this theory, reviewed elsewhere,[1] is overwhelming, and other views are not supported by sufficient evidence to merit consideration here.

Malignant blood cells may remain localized in one organ, producing a tumor infiltrating surrounding tissues. These forms of leukemia are spoken of as sarcomas, lymphosarcomas or myelosarcomas. More frequently the leukemic cells invade the blood stream, multiply by mitotic division and spread throughout the body, so that when the first symptoms appear the disease is widespread and appears to be systemic. Whether multicentric or unicentric at the start, in most instances leukemia appears to be systemic at the onset of the disease. The number of immature leukocytes in the circulating blood is, as a rule, of little significance. Interference with the function of organs which are infiltrated is the chief difficulty in leukemia. Irrespective of the primary site, all malignant blood cells have an affinity for the bone marrow, where they crowd out the other elements or otherwise interfere with the formation of normal granulocytes, erythrocytes and thrombocytes. Since leukemic cells themselves function as normal blood cells to only a limited degree, leukemia itself may be the indirect cause of an agranulocytic type of inflammation. The function of other infiltrated organs is similarly interfered with. The

1. Meulengracht, E., and others: Symposium on the Blood and Blood-Forming Organs, University of Wisconsin Press, 1939.

sites of infiltration vary considerably with different cases. The primary symptoms are referred to the bone marrow, brain, spleen, kidney or almost any other organ.

The causes of leukemia are unknown. Experimental studies in animals indicate that both intrinsic, that is hereditary, and extrinsic, or environmental, factors are responsible for it. The leukemias observed in man are of unknown etiology, with rare exceptions, e. g. cases occurring in persons exposed to x-rays or benzene. Neoplastic cells are not controlled by removal of the agent which has produced them; a knowledge of the etiology of leukemias might help in preventing the disease but promises little as regards treatment.

Leukemic cells, like neoplastic cells in general, are slightly more vulnerable to physical and chemical agents which injure normal blood cells; hence the decrease of the number of leukemic cells by properly adjusted doses in any part of the body is a feasible procedure. About this Dr. Forkner will speak to you.

TREATMENT OF LEUKEMIA

DR. ADE T. MILHORAT: Dr. Forkner will discuss the clinical aspects of the subject.

DR. CLAUDE E. FORKNER: One may adopt a more optimistic attitude in regard to the therapy of leukemia than is indicated by the term neoplasm, for it appears that in some cases of leukemia, at least, the process is reversible. The occurrence of spontaneous remissions in leukemia is an illustration. In these a full-blown picture of leukemia proved in biopsies of the bone marrow regresses until both the blood and the bone marrow structures return to normal. A few months later the condition recurs and the patient dies of it. The fact, however, that there is this reversibility introduces a hopeful element for the development of effective therapy.

Although leukemia is a fatal disease, much can be done about alleviating the symptoms and making the patients more comfortable. That applies especially to the chronic forms. Among the general measures which may be used to alleviate the symptoms are rest and regulation of activities. Patients with leukemia complain often of weakness. They may complain of feeling excessively tired. These frequently are manifestations either of the increased basal metabolic rate or of anemia. There may be symptoms referable to pressure of some enlarged organ on other important organs. Patients with leukemia should be guided in their activities, depending on their general physical state, their activities being limited to avoid undue fatigue and when they are in a state of remission again their activities being increased. One should not regard the leukemic patient as an invalid. Frequently I see patients with a diagnosis of chronic myelogenous leukemia or chronic lymphogenous leukemia whom the physician advises to stay in bed and to restrict their activities markedly. Even though they have some symptoms, rigid restriction of activities is undesirable. I think a patient with leukemia should be allowed activity compatible with his general state, with the anemia, with the symptoms of increased metabolism and with the enlargement of the spleen or liver. Often a patient with chronic leukemia can play golf, swim and engage in other activities almost to the extent of a perfectly well person.

One often is asked about food for patients with leukemia. Should they receive a special diet? This is not of particular value in leukemia. A number of my patients with chronic myelogenous leukemia, particularly the more intelligent ones, have themselves found that they feel better if they take large quantities of fats. Some patients have said that unless they have generous amounts of butter or cream they do not feel well. One patient said that she eats three times as much butter as any other member of the family, and if she does not eat butter she cannot do her work. The explanation may be that these patients have a high basal metabolic rate and that fats are a good source of energy. Also it is sometimes important to feed patients with leukemia at frequent intervals. Instead of three large meals they may perhaps have five or six small meals, the reason being that the spleen and the liver are at times so greatly enlarged that they encroach on the organs of digestion so that patients cannot fill up their stomachs without discomfort. In general, the diet of the patient with leukemia should be well balanced, as high in calories as the patient can tolerate and should have an adequate quantity of accessory food substances.

Frequently one is asked Should a patient with leukemia seek a more equitable climate? Should he go to Florida or to California? There is no evidence to suggest that climate has anything to do with leukemia, but it is advisable of course as far as possible to avoid respiratory infections. Perhaps under certain circumstances, particularly if the patient is subject to respiratory infections or sinus disease, he may do better in a climate where the weather does not change rapidly. Oral hygiene is also important in the treatment of leukemia. These patients are susceptible to infections about the teeth and the mucous membranes. This is particularly true in the later stages of chronic leukemia and in acute leukemia. One must be careful to have them cleanse their mouths gently. Conservative means should be employed in the treatment of any lesions of the mucous membranes, of the teeth or of the mouth. Frequently patients have toothache, and they go to their dentists before they go to their physicians. As you know, these patients have a special tendency to bleed; they may become almost exsanguinated as a result of a simple tooth extraction. Any operative procedures that are necessary should be carried out under careful supervision, preferably in the hospital, and if there is bleeding from the nose or from other mucous membranes only conservative measures should be taken. Transfusions of blood may be of value. Cauterization of bleeding areas should be done with great reluctance.

In a previous conference we covered the subject of the roentgen treatment of diseases of the blood; in that conference we discussed the treatment of leukemia in detail and we said something about the selection of cases for treatment. I want to repeat just two or three of those matters briefly: First, the fact that a patient has leukemia is not sufficient reason for immediate treatment with x-rays or with any other procedure. The treatment is essentially symptomatic. We cannot cure the disease by x-rays, benzene, arsenic or any other procedure. We treat patients in order to relieve their symptoms, and subsequently we try to anticipate the next relapse, treating them if we can before a relapse occurs. By careful observation of the blood, the basal metabolic rate and the patient's physical condition, we can often anticipate the onset of another relapse and forestall it by giving treatment before it actually occurs.

Patients with acute leukemia do not respond to any form of treatment as a rule; occasionally some improve-

ment is obtained, but it is evanescent and usually disappears in the course of a few days. Why some of these patients rarely have spontaneous remissions no one knows. All patients with chronic leukemia eventually come to a refractory state where no treatment is effective; where the cells in the bone marrow, in the blood and in the lymph nodes for some reason or other do not respond to roentgen treatment or to any other treatment. The treatment may decrease the number of cells but the patient may not be clinically benefited.

Although we treat patients with chronic leukemia fairly effectively with x-rays, radium, benzene and arsenic, these agents also are known to render individuals more susceptible to leukemia. This paradox may help one to understand why such agents fail to cure the disease.

Arsenic enjoys the reputation of being both the oldest and also the newest form of effective treatment of leukemia. Lissauer in 1865 first discovered that solution of potassium arsenite (Fowler's solution), which represents 1 per cent arsenic trioxide, was effective in reducing the leukocyte count and producing clinical betterment in patients with chronic leukemia. Cutler and Bradford at the Boston City Hospital in 1878 further studied the effects of this drug. They reduced the leukocyte count of a patient with chronic myelogenous leukemia from over a million cells down to 8,000 and produced dramatic betterment. When x-rays were found to be effective by Senn and others in 1903, the effects of arsenic were largely lost sight of because it was thought that x-rays actually constituted a cure for the disease. The opinion also developed that arsenic either had no effect at all in leukemia or that if it did have an effect it acted merely as a "tonic" and was beneficial in the anemia; but a great many workers felt that it had no specific effect on the leukemia. We have studied the effects of arsenic, particularly solution of potassium arsenite, and demonstrated rather conclusively that benefits accrue from treatment which are comparable to those of treatment with radium or with x-rays. A count can be brought from several hundred thousand per cubic millimeter down to normal. The anemia may completely subside. The basal metabolic rate can be reduced from + 40 or 50 to normal. The bone marrow can be reversed from a frankly leukemic state to marrow that can hardly be recognized as leukemic. The patient will gain weight and feel much better. The spleen and the liver, which may be many centimeters below the costal margins, can be reduced so that they are no longer palpable. All signs of remission are induced, and such effects occur regularly in patients with chronic myelogenous leukemia. The drug is not so effective in chronic lymphogenous leukemia, but neither are x-rays so effective in that form of the disease.

The method of giving solution of potassium arsenite is to begin with small doses. We usually begin with 0.2 or 0.3 cc. (about 3 or 4 minims) of the solution three times daily after meals, well diluted in some food substance like coffee or orange juice, in order to mask the drug. It must be taken immediately after meals and regularly; if doses are missed frequently, the effects are not satisfactory. The doses are then gradually increased by about 1 minim a day until 8, 10 or even 15 minims (0.5, 0.6 or 0.9 cc.) three times a day is given. The exact amount varies with different patients. Along about the tenth or twelfth day the leukocyte count begins to drop precipitously. Within a few days the patient begins to feel better, the anemia is lessened, and all the symptoms of remission become apparent. As soon as the leukocyte count reaches normal or near normal, the dose is gradually decreased by about the same rate of 1 minim (0.06 cc.) a day until the patient is taking 4 or 5 minims three times a day, and with that dose he can be maintained for many months, during which remission will persist. On the other hand, if the drug is discontinued abruptly, about three weeks later the leukocyte count will begin to rise and the patient will have another relapse. It is important to decrease the drug slowly just as it is to increase it slowly. We do not know exactly the reason for this, but it is an old observation which is borne out by recent studies. Minor manifestations of arsenic poisoning such as loss of appetite, slight diarrhea, perhaps slight nausea, chemosis of the conjunctiva and scaling and drying of the skin may be disregarded. More serious symptoms, such as peripheral neuritis, are rarely encountered, but when they are the drug must be discontinued.

Almost every clinic in the United States has discontinued the use of benzene in the treatment of leukemia, but I believe that this has been done without sufficient reason. I have seen a number of patients who have been successfully treated with benzene in doses of about 4 Gm. administered in capsules with olive oil by mouth daily. The evidence which has been presented against it, if reviewed critically, is found inadequate. The drug can be used effectively, but it must be used carefully. Recent studies by Kalapos, in which he has observed a large number of cases, indicate that the drug is worthy of use in leukemia.

AGRANULOCYTOSIS AND LEUKOPENIA

I do not think that agranulocytosis is merely an exaggerated form of leukopenia. I regard it as quite a different process. Acute agranulocytosis is something which comes on suddenly. It may appear on the basis of leukopenia or it may come on in a patient who has leukocytosis or leukemia. It is an acute episode with a definite syndrome, which then either goes on to death in about 70 per cent of the cases or to spontaneous or possibly induced recovery in 30 per cent of the cases.

Several measures have been advocated for its treatment. Friedemann as long ago as 1927 recommended roentgen treatment with small doses, one twentieth of an erythema dose, applied over the long bones, scapulas, sternum and pelvis, and claimed remissions in some cases. His group of cases was well selected and he tended to eliminate patients who had not been benefited within the first three days of treatment. Others have been unable to induce satisfactory remissions with this method. I do not think there is any good evidence that roentgen treatment, even though it is regarded as a stimulating dose, is of any value in the treatment of agranulocytosis. Frequently patients receive transfusions of blood, as it is thought that transfusions might supply leukocytes. Our own studies in agranulocytosis have shown that transfusions are of no value. In fact, in frequent counts of the blood we found that the white blood cell count was as a rule lower within two or three hours after the transfusions than it was before and that the leukocytes which are transfused disappear from the blood in the course of an hour or two. The studies which have been made of groups of cases, I think, do not demonstrate that transfusions are of any value in acute agranulocytosis. Dr. Reznikoff reported fifteen cases in which adenine sulfate was administered and he is going to say something about that later. Jackson, Parker and Taylor in 1932 suggested that pentnucleotide be given intramuscularly in daily doses of from 20 to 40 cc. in cases of agranulocytic angina,

on the basis of the theory that pentnucleotide or other nucleic acid derivatives might be effective in stimulating the bone marrow. Jackson's cases, again, were somewhat of a selected group, and I think that most clinicians feel now that perhaps the treatment with pentnucleotide is not as satisfactory as it was once thought to be. In his group 33 per cent of the patients died.

Liver extract has been given and thought to be effective, but there has not been any large series of cases in which the effectiveness has been proved. As a matter of fact there has been no satisfactory study of a treated group of cases of agranulocytic angina and a control group comparable as to age, nutrition, general state of health and blood picture in which any therapeutic agent has been shown to be beneficial. The most important factor in the treatment is, as Dr. Furth suggested, to remove the offending agent, if it can be found.

DR. MILHORAT: Would Dr. Reznikoff care to make a few remarks on agranulocytosis?

DR. PAUL REZNIKOFF: The term we prefer to use for this condition is not agranulocytosis. Although that is the most commonly accepted term, the better term I think is neutropenia or granulocytopenia because the neutrophils are the particular cells that interest us. Four factors have been considered instrumental in causing neutropenia. Dr. Furth has mentioned the first, namely certain drugs. I believe he omitted gold salts. A monograph written by Plum gives an account of the various drugs which tend to depress the bone marrow. Some workers believe that other factors are necessary. The patient must be susceptible before the drug can exert its effect. Other factors incriminated are undue fatigue, menstruation and possibly infection. In ordinary infections neutropenia is rare. Infections more commonly cause leukopenia but rarely neutropenia. Even though the total white blood cell count is very low, an adequate number of neutrophils is present in ordinary infectious leukopenia. In the typical attack of granulocytopenia, the decrease in the neutrophils precedes other phenomena. Kracke has demonstrated that the so-called agranulocytosis occurs before the angina.

As Dr. Forkner has indicated, prophylaxis is the most important aspect of the treatment of this condition. He has mentioned various agents that have been used. Watkins maintains that he has obtained good results with yellow bone marrow supplied by Armour. He gives it in doses of from 0.5 to 1 cc. I have given as much as 4 cc. of this oily extract by mouth three times a day, usually floated on some chilled tomato juice. Roentgen treatment is, I believe, dangerous, for while there is some apparent stimulation of the bone marrow due to transitory hyperemia, many of these patients show even more depression of the marrow after roentgen therapy than before. Liver extract has been given in doses similar to those used in the treatment of pernicious anemia, from 15 to 45 units a day intramuscularly, on the supposition that it might prove effective because in pernicious anemia the increase of the reticulocytes is accompanied by an increase of the white blood cells and polymorphonuclear cells. I believe that these two diseases are entirely different, however, and no good evidence exists that liver extract is effective. I agree with Dr. Forkner that transfusions are of no particular value, although they probably do no harm.

With regard to the nucleic acid derivatives, adenine sulfate is given intravenously in doses of 1 Gm. dissolved in about 25 or 30 cc. of hot saline solution three times a day for about three days. The compound is insoluble except in hot solutions, so we dissolve the 1 Gm. in boiling saline solution and give it as warm as the patient can endure, being careful that none of it gets into the tissues outside the vein, where it will cause necrosis.

Pentnucleotide is given intramuscularly. Occasionally it produces severe reactions. I give it in small doses of 1 cc. at first; if it produces no untoward effects, the doses are doubled until 10 cc. is given four times a day. About all of these agents one may say that they are not specific, nor is there any good evidence, in my opinion, that patients have ever recovered through their use. A good example of how difficult it is to evaluate treatment of this disease is the experience of Dr. Dameshek of Boston, who once told me that he had never lost a patient to whom he gave adenine sulfate and believed that my claims concerning this compound were too conservative. Six months later he told me that he had had twelve patients who died after it was used.

In the prophylaxis of this disease one should refrain from the use of those agents known to cause it. Aminopyrine can perhaps be dispensed with, without great loss to the patient, although some appear to be unable to obtain relief from menstrual pain or headaches with other drugs. Sulfapyridine and sulfanilamide are also included among the chemical agents which cause this disease. It would indeed be a great misfortune to attempt to dispense with these. However, their dangers would be greatly reduced if physicians were generally made aware of the possibilities of neutropenia and used them only where there is definite indication and in those cases in which the possibility of their proving effective is fairly strong.

DR. MILHORAT: Dr. Craver of the Memorial Hospital has been able to attend this conference.

DR. LLOYD F. CRAVER: In myelogenous leukemia one of the difficult problems is the case in which the spleen has been reduced by irradiation and, while it is still small, evidence of relapse appears in the blood count. What is one to do next? Should one irradiate the spleen, which is still small, or should one irradiate the bone marrow or large sections of the body or even the entire body? We do not follow any fixed rule. In some cases we have irradiated the small spleen again; in others we have irradiated the bones, although in general we are fearful of very much irradiation over the bones, and in other cases we have tried general irradiation or large sectional irradiation.

We have not used arsenic much, especially in recent years, and I wanted to ask Dr. Forkner what routine, if any, he has with regard to the administration of arsenic in relation to cycles of irradiation. Does he use it concomitantly with the irradiation or only in the intervals between cycles of treatment, or does he restrict the treatment of selected cases to arsenic or to irradiation?

I would like also to put in my word along with Dr. Forkner's about the idea of leukemia being a neoplasm. I cannot speak, of course, from the pathologist's point of view or from the point of view of one who has experimented with animals. I can speak only from the point of view of the clinician who has seen a good many of these cases. My impression about leukemia is very similar to my impression about Hodgkin's disease, namely that it begins as an inflammatory process or an overresponse to something or other on the part of the organism. In the beginning I feel that it is probably not a neoplasm. I think of those acute

cases that Dr. Forkner mentioned and I am inclined to think that in some instances it may be a reversible reaction; but then in many cases it does go on in later stages to what is probably a neoplastic process, just as in the case of Hodgkin's sarcoma. I even think of lymphosarcoma in the same way, and undoubtedly lymphosarcoma is commonly thought of as a malignant tumor; yet as a large number of those cases are seen certain cases are encountered in which it begins as an atypical low grade process hardly distinguishable from an inflammatory process. I wonder if this is not simply a short stage of passage between an inflammatory process and a true neoplasm. I think the same remarks can be applied to many forms of neoplasms, such as epidermoid carcinomas, which appear to begin as some sort of tissue reaction which goes over into a true neoplasm.

DR. FORKNER: We would do as Dr. Craver has done, namely individualize patients. If a long time has elapsed since the patient has had any irradiation and if enlargement of the spleen and changes in the blood are associated with increasing anemia, with an increased metabolic rate or with distress of any sort, I think that the thing to do is to go ahead and treat that patient again. Give him just enough roentgen therapy to produce a remission. I do not believe there is any evidence to indicate that large doses of x-rays frequently repeated are of any more value in leukemia than just enough treatment to control the disease.

DR. CRAVER: Where would you apply the treatment in such a case?

DR. FORKNER: I feel as you do about treating the bones of a patient with leukemia. I think that the anemia is less likely to be relieved promptly and that one is more likely to get serious thrombocytopenia than if one treats other structures such as the spleen or thorax.

The total irradiation I myself have had relatively little experience with, but I feel somewhat afraid of total irradiation of the body in leukemia. We have seen a few bad results in which even after very small doses, as little as 35 or 50 roentgens applied to the front or back of the body, there have been a very marked drop of leukocytes, severe thrombocytopenia and persistent anemia. I think one can control the treatment better by limiting it to some particular part of the body. I should like to know what your experience has been with regard to total irradiation in cases of chronic leukemia.

With regard to the question of arsenic plus irradiation or arsenic alone or irradiation alone, I think that most patients with chronic myelogenous leukemia will have a thoroughly satisfactory response with arsenic and that it is easier to control the treatment with arsenic than with x-rays. As a rule, the drug therapy is less expensive than roentgen treatment. The treatment can be given in places where there is no access to radiotherapy machines. I think that frequently therapeutic methods can be alternated with profit, arsenic being given at one time and radiation at another. Arendt and Gloor in their series of cases reported in 1932 used that sort of treatment, giving arsenic plus radiation and arsenic alternated with radiation. They thought that they had better results and that they had actually prolonged the lives of the patients more by that means than they had by either agent alone.

DR. CRAVER: Total irradiation was first proposed between 1905 and 1907 in Germany by Dessauer and a collaborator, but I do not believe they put it into practical use. It was not until after the war that some European workers began to irradiate the whole body of a patient for various radiosensitive processes, particularly the lymphoid diseases, leukemia and so on. The method has been mostly that known as the spray therapy. One simply backs off an x-ray tube to a sufficient distance, a meter or a meter and a half, so that its rays can encompass all or nearly all of the body. Our experience at the Memorial Hospital has been limited almost entirely to the Heublein method. We have a special unit consisting of two rooms with the x-ray tube mounted in the ceiling or between the rooms. The patients stay there in bed day and night and are exposed to radiation of a very low intensity, about 1 roentgen per hour, or now 1½ roentgens, although I think that perhaps is a little too rapid. Therefore with the time out for nursing care, meals, visiting and so on, they get only about 15, 18 or perhaps 20 roentgens in a whole twenty-four hour period. If one were to give it intermittently with an x-ray tube one would deliver from 10 to 25 roentgens within a few minutes, which is considerably more of a shock to the organism, I believe. Total irradiation is a method which has come to stay in several fields of the radiosensitive diseases. In leukemia we have been more impressed with its results in chronic lymphogenous leukemia than in myelogenous leukemia. There are workers who maintain that with this method results can be obtained in the resistant case, the roentgen-fast case, of myelogenous leukemia; that is, the case with the big spleen that cannot be reduced any further with local irradiation. In these, total irradiation, they state, makes the spleen go down. I have never seen that happen, although I have no reason to doubt that it may take place in some cases. The result that impresses me is the effect on the blood count and not the effect on areas of lymphocytic or myelocytic infiltration. It has seemed to us that in lymphogenous leukemia we get results that are worth while, provided we do not carry the dose too far. I do not think we should exceed a total of 100 roentgens, which with the Heublein method would take about five or six days of treatment. We can discontinue whenever we see danger signals.

"GRANULOCYTOPENIA" VERSUS "AGRANULOCYTOSIS"

DR. FORKNER: I should like to say one more word in disagreement with Dr. Reznikoff about the use of the terms neutropenia or granulocytopenia, instead of agranulocytosis. Agranulocytosis is such an acute episode that I prefer the term acute agranulocytosis. It is not just neutropenia. There is a neutropenia in pernicious anemia, in Banti's syndrome, in malaria and in a great many other diseases, but I think agranulocytosis deserves a little more distinction than is suggested by the term neutropenia or granulocytopenia.

DR. REZNIKOFF: I am certainly in favor of distinguishing it, but we call it acute neutropenia. We put in the term "acute." The trouble in using agranulocytosis is that there are other cells that are granulocytes such as monocytes, and they are not always absent. But the distinctive feature of this acute condition is the fact that the principal cells which are depressed, and markedly depressed, usually below 10 per cent, are the neutrophils. I think it is also incorrect to use the term "angina."

DR. HARRY GOLD: I think the difference in terms used may have some bearing on the subject of therapy. Dr. Forkner said that about 70 per cent of patients with

acute agranulocytosis die, but it is my impression that in the group that would naturally fall under the designation granulocytopenia, the mortality is not nearly so high. Naturally it is the concept behind the names that matters. Most patients who have a low white blood cell count and a low neutrophil count and nothing else, I believe, recover. These could be considered cases of neutropenia or granulocytopenia. But Dr. Forkner has applied the term acute agranulocytosis to a condition which has a mortality of 70 per cent. Is there here only a difference in the severity of the disease or are some of the conditions included under the name neutropenia entirely different diseases bearing only superficial similarities to those included under the name acute agranulocytic angina? The reason I press the point is that the efficacy of a therapeutic agent can be evaluated only on the basis of the natural course of the disease or its mortality. The literature records several false steps in the attempts to treat so-called agranulocytosis. It is fairly easy to be misled in a disease which has a natural recovery rate of 70 per cent. The matter is otherwise in a disease with a natural mortality rate of 70 per cent. Which does this disease have?

DR. REZNIKOFF: The difference in the mortality figures for these conditions is due to the difference in the severity of the cases included in different groups that have been observed. Dr. Forkner and I refer to the same disease, although we prefer to apply different names to it.

DR. FORKNER: When I referred to the mortality of 70 per cent I had in mind not simple neutropenia but the more severe acute agranulocytosis.

DISCUSSION OF QUESTIONS

STUDENT: I should like to ask Dr. Forkner if platelets could not be used in leukemia as a possible diagnostic or prognostic index?

DR. FORKNER: Marked reduction or the absence of platelets in leukemia is on the whole a poor sign. One can expect less from therapeutic agents when the platelets are low in number. I think it is very important to consider them in treatment or in diagnosis, and no smear is adequately studied unless a statement is made about the platelets. Both in acute and in chronic uncomplicated lymphogenous leukemia there is a reduction in platelets. In myelogenous leukemia usually their number is normal or increased.

DR. MILHORAT: I gather that the basal metabolic rate is pretty important. What relation, if any, has the basal metabolic rate to the white count?

DR. FORKNER: Only in patients who have high white counts is there any relationship. A patient with leukopenia or with so-called subleukemic leukemia may have a very high basal metabolic rate. In that case there is no relation. But when a patient has a high white count the basal metabolism will vary more or less directly with the leukocyte count. A closer correlation is seen between the basal metabolic rate and the degree of immaturity of the cells.

DR. WALTER MODELL: Do you find arsenic of any value when the leukemic patient no longer responds to irradiation?

DR. FORKNER: Usually the patients who respond well to arsenic respond well to irradiation; those who take low doses of arsenic will take low doses of irradiation. Occasionally a patient will respond to arsenic who will not respond to irradiation and vice versa, but that is not the rule. We have no indication of the mechanism by which arsenic is effective in leukemia. It is a good problem.

STUDENT: Is leukopenia a contraindication to the use of such substances as sulfanilamide, which are known at times to cause it?

DR. FORKNER: I do not think so, but you will find difference of opinion on that. If the leukopenia is due to sulfanilamide then put out the red flag, but if the leukopenia is due to the infection I do not think it is a contraindication to the use of sulfanilamide.

SUMMARY

DR. MILHORAT: Dr. Travell, will you add a few words in summary?

DR. TRAVELL: The conference today dealt with the therapy of two widely diverse groups of disorders of the white blood cells: those in which there is depression of the leukopoietic tissues on the one hand, and those in which there is excessive multiplication of the leukocytes, that is, the leukemias, on the other hand.

The terminology for the former group apparently needs some clarification, for the term agranulocytosis has been used to indicate an acute clinical syndrome which is usually fatal and also to apply to milder grades of granulocytopenia or neutropenia, from which the patient often recovers spontaneously. This uncertainty as to the expected mortality rate makes it difficult to evaluate the efficacy of the variety of therapeutic agents which have been used in the treatment of these conditions.

In agranulocytosis, granulocytopenia or neutropenia, the first aim of therapy is to remove the cause, and removal of the cause is usually all that is necessary to effect a cure. The etiologic factors include the use in hypersensitive individuals of certain drugs containing the benzene ring, such as aminopyrine, sulfanilamide, sulfapyridine and arsenicals, bacterial toxins, and x-rays and radium. In some instances the cause is obscure. The second aim of therapy is to stimulate the production and maturation of the granulocytes. For this purpose transfusions, liver extract and bone marrow stimulating agents, such as adenine sulfate and pentnucleotide, are of uncertain value. "Stimulating" doses of x-rays are of no value and may be dangerous.

The treatment of leukemia presents a different type of problem. It is generally believed that this is a neoplastic disease and, once initiated, removal of the cause would not in this case effect a cure. Although the patients with leukemia are rarely if ever cured, it is possible to relieve their symptoms. Remissions can be produced by suitable doses of x-rays or of arsenic or benzene. All of these measures tend to depress the bone marrow and thereby reduce the number of circulating white cells and the size of the tumor masses which are frequently the cause of symptoms. In the refractory stages of the disease a decrease in the number of white blood cells in the blood, however, is not always correlated with clinical improvement. It is possible that arsenic and irradiation may be combined with some advantage. Stress was laid on nonspecific measures which help to preserve the best possible state of well-being in the leukemic patient, such as the suitable restriction of activity, a high caloric diet, control of respiratory infections, attention to oral hygiene, and the avoidance of trauma because of the tendency to bleed. Probably the most important feature is the adaptation of therapy to the individual patient.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

HOWARD A. CARTER, Secretary.

CLARK HYDROTHERM NOT ACCEPTABLE

Manufacturer: Clark Electrical Equipment Company, Warren, Pa.

The Clark Hydrotherm, described in the advertising matter as a "humid air Fever Box," was not submitted to the Council for investigation; this report is based therefore on the advertising and promotional matter distributed by the firm.

A giant rubber hot water container, said to be 30 by 78 inches, called the Hydroelectric Mattress, appears to be the main feature of the device. As described in the advertising, "It is inflated with 10 gallons of water and air which is heated to any desired degree thermostatically. In the lower section of this mattress is a unique heating unit so designed as to operate as 'black heat' yet impart over the entire lower surface sufficient heat to raise the temperature of the water and air to any desired degree." It is claimed that "No other form of mattress construction offers the superb comfort which patients enjoy with our product. The patient floats upon this mattress as does a ship upon the sea."

This mattress is placed on a bed assembly. In the base of this assembly, a "unique vapor generator" is claimed to maintain a 75 per cent humidity in the cabinet. The enclosing cabinet or hood, on which are located various indicators and gages, is apparently used only when the temperature or fever is being induced. It is stated, "A very important feature is the fact that ⅔ of the enclosing cabinet is mounted upon rollers so that it can be moved back over the foot end after the desired degree of fever is obtained. Fever can be maintained for any number of hours with cabinet moved back as the conduction of heat from the Hydroelectric Mattress is sufficient to hold the body temperature."

The advertising appears to be quite evenly proportioned between describing the mechanical virtues of the apparatus and its money-making possibilities. The physician is informed that "Producing results with fever will definitely expand your practice and income."

The following is quoted from promotional matter distributed by the firm:

"Here is a field, doctor, waiting—untouched—and the majority of these patients are prepared to pay well for definite results. You know that the average physician does not warm up to physical measures of heating—so-called machine medicine—yet FEVER is best developed by man-made methods and not with serums of foreign substances injected into the blood stream.

"With Government appropriation for a huge expansion of the Health program plus the present program to fight the spread of Venereal diseases—YOU have a virgin opportunity to step out front—become a leader in making FEVER available to those in your community who are waiting for some progressive doctor to install such a department.

"With the HYPOTHERM you can treat three to six patients per day—because you can develop a fever of 101 or 102 in less than 90 minutes—then after an hour's rest the patient can leave. These frequent passive treatments will be appreciated by hundreds who would rather come to YOUR OFFICE than go to a hospital—therefore Doctor—make room for this service; it will do more to PUT YOU OVER in your community than any investment you can make.

"Don't pass up this opportunity—don't say you haven't room—do as any businessman would do—MAKE ROOM for a profitable department—in a few years you'll be glad you did—people will be coming to you from far and near—we know they will be because we've sold our machines on the PAY OUT OF INCOME PLAN all during the depression and we know that doctors will pay us—when they are adding to their income—expanding their practice with our investment."

This promotion has the flavor of advertising copy used to distribute money-making amusement devices rather than professional equipment for a physician's office or a clinic. There is even described a "meter-matic plan" whereby a certain number of coins are deposited in the apparatus each day until it is paid for.

The practice of fever therapy, in the opinion of the Council, should be limited to those who have been especially trained in this highly specialized field. Much instruction and practice in a fever clinic are required before such training is sufficient.

One piece of advertising, which appears to be a reprint, is titled "Pasturizing the Blood (Pyretotherapy with Conductive Heat)." On examination it is found that the author, said to be a well known physician, is not named, nor is the "leading medical journal" in which it is claimed that the article appeared.

The present Clark Hydrotherm, or Thermobath as it is sometimes called in the advertising, has superseded the more costly Clark Hyperpyrexator, according to the firm. Many unwarranted claims were made for the Clark Hyperpyrexator.

"Dr. Warren's Infra-Red Sitz Bath," marketed by Electrical Research Laboratories, was found not acceptable by the Council, as reported in THE JOURNAL, Sept. 14, 1935, page 881. According to correspondence and advertising, W. W. Clark is president of both the Electrical Research Laboratories and the Clark Electrical Equipment Company, and each is located in Warren, Pa. "Dr. Warren's Sitz Bath" consisted of a stool having a ringlike seat with a heating element in the base. It was claimed that this apparatus had many therapeutic benefits, and it was said to be a "Convenient and Effective Method of Rejuvination," which would "Restore Physical Vigor." The device was advertised directly to the public.

The Council on Physical Therapy declared the Clark Hydrotherm not acceptable for inclusion in its list of accepted devices.

Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

ANNUAL MEETING OF THE COUNCIL ON PHARMACY AND CHEMISTRY

The Council on Pharmacy and Chemistry of the American Medical Association held its thirty-fifth annual meeting at the Association headquarters March 8-9, 1940. Those in attendance were Drs. David Barr, J. Howard Brown, S. W. Clausen, H. N. Cole, C. W. Edmunds, Morris Fishbein, E. M. K. Geiling, Paul Nicholas Leech, Perrin H. Long, G. W. McCoy, Stuart Mudd, E. M. Nelson, W. W. Palmer and Elmer L. Sevringhaus. In addition, the following members of the Council on Foods attended the meeting: Dr. George R. Cowgill, Dr. Arild E. Hansen (proxy for Dr. Irvine McQuarrie), Mr. Culver S. Ladd, Dr. James S. McLester, Dr. Tom D. Spies, Dr. Russell M. Wilder and Dr. Franklin C. Bing.

Dr. Torald Sollmann was reelected chairman of the Council and Dr. W. W. Palmer was reelected vice chairman.

Among the many items discussed, the following may be of interest both to physicians and to manufacturers:

Use of Term "Digitalis Unit."—The Council voted that a special committee be appointed to consider in extenso the digitalis unit and report back to the Council. In the discussion it was emphasized that digitalis, or anything that purports to be digitalis, is an official drug and, by that token, it must be standardized according to the methods laid down by the U. S. Pharmacopeia. If there is a demand for another standard, that standard may appear on the label in addition to the U. S. P. standard, provided the labeling of the second standard is not misleading. It was also emphasized that representations may be made to the U. S. Pharmacopeial Revision Committee for reconsidering the standards of digitalis preparations if that is necessary.

Councils' Committee on Contraceptives.—The Councils' Committee on Contraceptives made a progress report concerning certain articles that have been authorized for publication. The

Council voted that certain recommendations of the Committee be adopted by the Council on Pharmacy and Chemistry and referred to the Board of Trustees for action.

Change of Name "Thiamin Chloride."—The Council voted to adopt the pharmacopeial term "thiamine hydrochloride" to replace the term suggested by the discoverer, i. e. "thiamin chloride." The manufacturers of accepted preparations, however, will be given a suitable period of time in which to use up the old labels bearing the name "thiamin chloride."

Proposed Articles on Glandular Therapy and Physiology.—The Council received a report from the committee in charge of the proposed new series of articles and authorized the Secretary's office to approach certain persons with the request that they contribute to this series.

Present Status of Pneumonia Therapy.—It was pointed out that the difficult question at the present time in determining the preferred treatment of pneumonia is whether or not the best plan is to use sulfapyridine alone, serum alone, or serum and sulfapyridine. It was the general consensus that there is not sufficient information yet available to determine the value of combined serum and sulfapyridine compared with adequate serum therapy alone or with adequate sulfapyridine therapy alone. Furthermore, there enters into the equation the relative cheapness of sulfapyridine therapy in comparison with serum therapy. It was the general consensus of the Council members that the practice of typing should be continued for information, both in relation to treatment and for statistical purposes. In early cases of pneumonia and when typing has been employed it is probably best to give a specific antipneumococcic serum, at the same time (followed by the specific carbohydrate test to determine if the serum is present in sufficient amounts), this to be followed by the use of sulfapyridine, with the caution not to stop the administration of sulfapyridine too soon in order to avoid late complications. This statement, however, is to be looked on simply as a tentative statement based on the present evidence. As further data become available the Council will be in a position to make more positive statements.

The Council also voted to accept type III rabbit antipneumococcic serum for a period of one year only, and authorized publication of a report to the effect that the higher types of rabbit antiserums are under consideration. Furthermore, the Council will consider with the view to acceptance the carbohydrate material for skin testing and treatment in conjunction with antipneumococcic serums (Francis test).

Solution of Zinc Insulin Crystals.—The Council concluded that a statement should be prepared announcing recognition of solution of zinc insulin crystals for inclusion in New and Nonofficial Remedies.

Antiseptics, Bacteriostatic Agents, Preservatives and Disinfectants.—The Council again considered the problems relating to these preparations and the misunderstandings which arise concerning these terms. At the same time it again discussed the inadequacy of the phenol coefficient test for the evaluation of antiseptics and disinfectants. The referee was authorized to formulate a report for the consideration of the Council and, if possible, to consult with the federal authorities concerned with these questions.

Catgut Suture Investigation.—A progress report was made concerning the further investigation of catgut sutures. It is anticipated, however, that another year of investigation will be required before the Council may be in a position to publish the results of the work which is being undertaken under its auspices.

Advertising Brochures.—The Council discussed the question of the increasing number of large size brochures dealing with proprietary drugs. In this form of advertising the commercial houses take on themselves the task of educating the physician in the fields to which their products pertain. For instance, a recent brochure contained no less than sixty drawings of surgical procedures; others attempt to cover in elaborate detail such fields as those of endocrine or vitamin therapy. (The writers of these enlarged pamphlets discuss as many usages as possible for the product which they are promoting.) Some members of the Council felt that this type of advertising material is not to be commended and that pharmaceutical houses should confine their advertising material to less lengthy descriptions of the product and the technic used. On the other hand, it was pointed out that in some restricted fields textbooks on therapeutic problems are not sufficiently up to date and that in such instances these brochures may fill a need. It was voted that a special committee be appointed to inquire into the matter of advertising brochures and report to the Council, especially in regard to the abuses.

Pharmacopeial Convention.—The Council members discussed the forthcoming pharmacopeial convention with a view to enlisting the aid of the medical interests to attend the convention in order that good progress might be made in the final elaboration of the next pharmacopeia.

Rearrangement of Articles on Serums and Vaccines.—The Council members voted to revise and rearrange the New and Nonofficial Remedies chapter on serums and vaccines.

So-Called Lipoid Pneumonia.—The Council authorized a review to be made of the lipoid pneumonia problem, on the basis of which the Council might again consider what action to take in the case of nasal sprays in which liquid petrolatum is the vehicle.

Therapeutic Research.—The Council voted that the Committee on Therapeutic Research be thanked for its painstaking effort and for the active productivity of the work which it fosters. The report of the committee appears in the annual Reports of Officers, THE JOURNAL, May 11, 1940, p. 1918.

Permissible Claims for Vitamins.—The Council considered the "Status of Permissible Claims for Vitamins" as given in New and Nonofficial Remedies. It was the opinion of the Council that with a few exceptions these claims as they stood were applicable today. The Council ordered, however, that revisions be made in the permissible claims for riboflavin, nicotinic acid and pyridoxine (vitamin B_6), and that after the referees for these preparations have sent in their proposed alterations these be passed on by the Cooperative Committee on Vitamins with the view of later publishing a revised edition of the pamphlet entitled "The Status of Certain Questions Concerning Vitamins," and concordant revision of the statements in New and Nonofficial Remedies.

Nomenclature of Vitamins.—The Council voted to accept the terms "pyridoxine" and "pyridoxine hydrochloride" for the substances known as vitamin B_6 and vitamin B_6 hydrochloride, provided the nomenclature met with the approval of the American Society of Biological Chemists and the American Institute of Nutrition. The meetings of these organizations were to follow that of the Council (an official announcement of the Council on these names was published in THE JOURNAL, June 15, 1940, p. 2387).

The Council also discussed the term "halibut liver oil with viosterol" for a product containing halibut liver oil with viosterol and other fish liver oils. Such preparations have generally been diluted with cod and other fish liver oils to adjust the vitamin A content. The addition of such oils to a product sold under the labeled name "halibut liver oil with viosterol" will make the product subject to action under the misbranding provisions of the Federal Food, Drugs and Cosmetic Act even though the presence of the added ingredients is declared elsewhere on the label. The present definition for halibut liver oil with viosterol, as given in New and Nonofficial Remedies, is as follows:

> Halibut liver oil to which has been added sufficient viosterol (irradiated ergosterol) to assure a potency of not less than 10,000 vitamin D units (U. S. P.) per gram; the halibut liver oil used is adjusted (when necessary) to have a vitamin A potency of not less than 44,800 units (U. S. P.) of vitamin A per gram by the addition of fish liver oils from one or more of the species Gadus morrhua, Ophiodon elongatus and Anoplopoma fimbria.

The Council voted that this be changed and that the definition of the future editions of the New and Nonofficial Remedies be:

> Halibut liver oil-N. N. R. to which has been added sufficient viosterol (activated ergosterol) to assure a potency of not less than 10,000 U. S. P. units of vitamin D per gram.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JULY 13, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

CHEMICAL CHANGES IN THE BLOOD

The value of an understanding of the chemical changes that take place in the blood in disease has long been recognized. The data obtained as a result of biochemical analysis serve to supplement the information which the clinician may obtain in other ways. At present means exist for determining more completely than ever before changes in the blood that are encountered in disease. Ample application in the various branches of medicine is found, moreover, for all the knowledge obtainable concerning deviations from the normal in protein, carbohydrate, fat or inorganic metabolism as well as for aberrations of endocrine, renal or hepatic function. The literature dealing with clinical biochemistry is extremely voluminous; reports which discuss and correlate the results of investigative activity in this field are therefore welcome. In a recent review of this type, Myers and Muntwyler [1] draw attention to developments of the past few years with regard to chemical changes in the blood and to the clinical significance of these changes.

The clinical significance of wide excursions from the normal of the sugar content of blood is evident, yet many of the methods used to determine this constituent are rather nonspecific. Even the values obtained with the aid of the widely used Folin-Wu method are actually much higher than the values for the true sugar content of blood. With the help of methods now available, the true sugar content can be accurately determined. In estimations giving normal or elevated values, however, it is considered by many to be unnecessary to employ methods yielding the true blood sugar values, and procedures such as that of Folin and Wu are still commonly employed. In the latter case, of course, the limitations of the method are properly considered in the interpretation of the analytic results. However, when hypoglycemic blood is examined for sugar it is important to know its true carbohydrate content, because in this case the error occasioned by the presence of nonsugar reducing materials in blood is relatively great.

Variations which occur in the lipid content of blood in normal pregnancy, diabetes, certain renal conditions and pernicious anemia are comparatively well known and appreciated. In recent years the value of plasma cholesterol estimations in thyroid disease has been investigated [2] and the usefulness of plasma cholesterol and cholesterol ester determinations in liver disease has been emphasized.[3] The association of hypercholesterolemia and hyperbilirubinemia in obstructive jaundice has likewise received attention.[4] The serum pigments themselves have been of interest for many years and both the icterus index and the van den Bergh reaction have found extensive clinical use. The possible influence of carotenemia on the icterus index has merited notice, and some time ago Nation and Myers [5] came to the conclusion that only in cases of marked carotenemia, such as might be encountered in some diabetic patients, is the validity of the icterus index affected. Carotenemia observed in patients with diabetes mellitus may be due to the inability of the organism to convert carotene to vitamin A.[6]

With regard to the proteins in blood, it is interesting to note that the gasometric method of Van Slyke for the determination of the oxygen capacity, and hence the hemoglobin content, of blood has proved extremely useful. The simplicity of the method has also made it admirably suited to checking standards used in the determination of hemoglobin by colorimetric methods,

1. Myers, V. C., and Muntwyler, E.: Chemical Changes in Blood and Their Clinical Significance, Physiol. Rev. **20:** 1 (Jan.) 1940.

2. Hurxthal, L. M.: Blood Cholesterol in Thyroid Disease: Analysis of Findings in Toxic and Nontoxic Goiter Before Treatment, Arch. Int. Med. **51:** 22 (Jan.) 1933.

3. Epstein, E. Z.: Cholesterol Partition of Blood Plasma in Parenchymatous Diseases of Liver, Arch. Int. Med. **47:** 82 (Jan.) 1931; Cholesterol of Blood Plasma in Hepatic and Biliary Disease, ibid. **50:** 203 (Aug.) 1932.

4. Epstein, E. Z., and Greenspan, E. B.: Clinical Significance of Cholesterol Partition of Blood Plasma in Hepatic and in Biliary Diseases, Arch. Int. Med. **58:** 860 (Nov.) 1936.

5. Nation, E. F., and Myers, V. C.: Carotenemia: Its Influence on Validity of Icteric Index, Proc. Soc. Exper. Biol. & Med. **31:** 620 (Feb.) 1934.

6. Brazer, J. G., and Curtis, A. C.: Vitamin A Deficiency in Diabetes Mellitus, Arch. Int. Med. **65:** 90 (Jan.) 1940.

and directly or indirectly the gasometric procedure has facilitated the accumulation in all parts of the world of a vast amount of accurate information on the hemoglobin concentration of human blood. The value of estimations of serum proteins in the various forms of renal disease is generally recognized, and of late considerable attention has been paid to serum colloid osmotic pressure. Concerning the nonprotein nitrogen constituents of blood, Myers and Muntwyler indicate that nonprotein and urea nitrogen are probably still regarded as furnishing more information of diagnostic or prognostic import as far as the kidneys are concerned than any other single determination, although elevated values may sometimes be attributed to other causes. Regarding renal function tests a comparison of the blood urea clearance test with the blood urea and blood creatinine content alone, as well as with the phenolsulfonphthalein test, shows that the blood urea clearance usually falls below 50 per cent of its normal value before any of the other three values shows any abnormality.[7] The employment of the blood urea clearance test as a reference test in studies of renal function seems to be amply justified. The uric acid content of blood continues to receive attention, particularly in connection with gout, and the possible clinical importance of guanidine in the blood has attracted renewed interest with the development of an improved method for its determination. High values for guanidine in blood have been reported among other conditions in severe toxemias of pregnancy, in cases of epilepsy and in some cases of liver disease.

In addition to a consideration of the organic constituents of blood, the various inorganic materials have been increasingly studied in health and disease. Changes in the blood with regard to its content of sodium, potassium, magnesium and calcium among the cations and of bicarbonate, chloride and phosphate among the anions, in particular, are encountered in numerous clinical conditions. Even enzyme determinations are found to be clinically significant. Thus, estimations of plasma phosphatase activity are of especial value in the detection of latent or active rickets.

Each patient presents a problem which cannot be appreciated solely on the basis of dissociated laboratory studies.[8] Moreover, if any value is to be attached by the clinician to information obtained by the chemical analysis of blood it is imperative that he be fully aware not only of the significance which the results might have but also of the limitations of the methods used to supply the information. However, when properly interpreted a knowledge of chemical changes in the blood as revealed by analytic methods is of much clinical value. With the advent of a fuller understanding of the changes that occur in the blood in disease, the position of the laboratory as a helpmeet in medicine may be even more prominent than it is now.

7. Van Slyke, D. D., and others: Studies of Urea Excretion: Comparison of Blood Urea Clearance with Certain Other Measures of Renal Function, J. Clin. Investigation **8**: 357 (April) 1930.

8. Cantarow, Abraham, and Trumper, Max: Clinical Biochemistry, ed. 2, Philadelphia, W. B. Saunders Company, 1939.

POSTGRADUATE TRAINING IN CRIMINAL PSYCHIATRY

A Pennsylvania fellowship plan for intramural training in penal psychiatry has been formulated,[1] pursuant to recommendations of the Medical Society of the State of Pennsylvania,[2] by a joint medicolegal committee of the Philadelphia County Medical Society and the Philadelphia Bar Association. The plan has already been endorsed by the Philadelphia Psychiatric Society, the Pennsylvania Psychiatric Society, the College of Physicians of Philadelphia and the board of directors of the Philadelphia County Medical Society.

The joint medicolegal committee recognizes the need for education of the criminologist as well as rehabilitative education of the criminal offender. By its plan it hopes to provide an educational institution for the training of personnel and the development of quality research in the field of penal psychiatry and thus render more probable of success any scientific remedies which the state legislature may or has set up for various aspects of crime. The committee believes that its plan satisfies the essentials for training qualified persons in criminal psychiatry since it contemplates (1) the creation of fellowships in penal psychiatry, (2) the use of penal and correctional institutions as clinical laboratories and (3) the identification of the fellowships with some institution of learning.

The Pennsylvania plan is to be administered by a committee representing three departments of the University of Pennsylvania—the Department of Psychiatry, the Graduate School and the Law School—and the Eastern State Penitentiary. The fellowships are for a term of two calendar years and carry stipends of $2,600 the first year and $3,000 the second year, with additional allowances for clerical services. To qualify for such a fellowship a candidate must (1) be a male not over 35 years of age, (2) be a graduate from an accredited medical school, (3) have served an accredited internship, (4) possess a sound psychiatric background consisting of at least two years of acceptable previous psychiatric training and (5) possess acceptable character endorsements. The tentative curriculum prescribed for a fellow consists of study in the law, medical and graduate schools of the University of Pennsylvania, experience and observation at the Eastern State Penitentiary and in the courts, and participation in intramural clinical psychiatric problems related to classification, discipline, rehabilitative treatment and parole of criminals.

The committee is confident that its plan will not only accomplish its primary purpose of training competent personnel in criminal psychiatry but also improve the

1. Report on the Pennsylvania Plan (Intramural Training in Penal Psychiatry), Joint Medico-Legal Committee of the Philadelphia County Medical Society and the Philadelphia Bar Association, March 1940.

2. Minutes and Proceedings of the Eighty-Ninth Annual Session of the Medical Society of the State of Pennsylvania, Pittsburgh, Oct. 2-5, 1939, approving the Report of the Committee on Psychiatric Services to the Criminal Courts, Pennsylvania M. J. **43**: 293 (Dec.) 1939.

general status of psychiatric expert testimony and bring closer together the legal and medical professions, the University of Pennsylvania and state penal institutions to the end that all four may more effectively serve the needs of the community. The committee is to be commended for its timely efforts in blazing this much needed trail in the field of penal psychiatry.

Current Comment

EXPERIMENTS IN CANCER REPORTING

More than 12,000 cases of cancer have been reported since January to the Division of Cancer Control of the New York State Department of Health, according to a press release [1] dated May 27. This has come about through "prompt and adequate response of the medical profession in upstate New York in reporting cancer under the new cancer reporting law." Health department officials regard this as the first successful venture of its kind anywhere in the country and probably in the world. The reports are made by physicians, hospitals and laboratories and are of increasing scientific value because in more than 70 per cent of cases they are accompanied by data from the pathologic laboratory regarding the microscopic character of the tumor. These cancer reports are being handled "with the greatest possible care with respect to their confidential nature and they will be used for scientific analysis only." Unexpectedly, benign tumors and other benign conditions are being reported to the extent of more than a thousand cases a month; these reports may be of use in establishing statistical information as to how frequently a malignant condition may supervene in apparently benign growths. The practical working of a law requiring reports of a noncommunicable disease for statistical, educational and control purposes will be watched with interest by physicians everywhere. Already it is stated that the number of cases reported "compares favorably with results obtained in the past by expensive special surveys carried out to gather similar data."

HONORING DR. S. BURT WOLBACH

The current July issue of the *Archives of Pathology* is dedicated by his present and former pupils and associates to Dr. S. Burt Wolbach, of Harvard Medical School, where for thirty years he has served, in a distinguished manner, first as assistant professor and later as associate professor of bacteriology, then as associate professor of pathology and bacteriology, and since 1922 as Shattuck professor of pathology. In this large issue of the *Archives* are numerous scientific papers which indicate the broad field of study in which Professor Wolbach's students and associates have engaged and the far-reaching effect of his stimulating leadership in this field. Although for twenty years he has been pathologist to the Peter Bent Brigham Hospital and for a longer period to the Boston Children's Hospital, and to other hospitals, he also has vigorously carried on with his associates numerous researches, some of which disclose previously unappreciated opportunities for cooperation with workers in other fields. Especially notable are his researches on typhus, Rocky Mountain spotted fever, and the vitamins. Most interesting is the sketch of Dr. Wolbach's career, written by Prof. Walter B. Cannon as an introduction to this special issue. Dr. Wolbach, now 60 years of age, was born at Grand Island, Neb., where his early years were spent on the range in association with alert and hardy men whose enterprise helped to build Western civilization. Horseback riding today remains one of his chief recreations. To see Burt Wolbach and his favorite horse, Professor Cannon says, is a beautiful revelation of both human and equine nature. A morning ride, rain or shine, still keeps him physically fit for the strenuous work of the day—teaching, attending routine duties in school and hospitals, eagerly engaged in various research, and fulfilling his deep sense of obligation by guiding his disciples along old paths and toward fresh ventures in pathology. Wherever he has labored in hospitals and laboratories—in Boston, in Albany and in Montreal—his kindness and helpfulness have made for him devoted friends.

PULMONARY TUBERCULOSIS AFTER HEALED PRIMARY COMPLEX

A recent report by Fellows,[1] based on serial chest roentgenograms of 3,179 office employees from 1926 to 1938, introduces interesting evidence regarding the pathogenesis of tuberculosis. Fellows divided the group into those whose x-ray examinations showed (1) an average healthy or normal chest, (2) an apparently healed primary complex, and (3) a lesion requiring further study. In calculating the comparative incidence of the development of tuberculosis in the first two groups, the number of years of life under observation at each year of age was tallied by sex and note was made of the age at which tuberculosis was first detected. There were 2,536 persons in the average healthy or normal chest group and 449 in the healed primary complex group. Fifty in the first group acquired tuberculosis subsequent to this first roentgenogram; seven in the second group, whose first roentgenogram showed healed primary complex, also acquired tuberculosis. Thus it appeared that there was no greater tendency toward tuberculosis in those with healed primary complex than in those with chests roentgenographically normal. Moreover, it was clearly apparent from the entire study that apparently healthy working adolescents and adults frequently have conditions and diseases in the lungs which are unrecognized by the usual clinical examination and that an examination of the lungs cannot be considered complete without a fluoroscopic or roentgenographic examination. The latter conclusions have now been so thoroughly substantiated in numerous studies that they can be considered, for practical purposes, as clinically proved.

1. New York State Dept. of Health, Albany, N. Y., News Service, May 27, 1940, Edward S. Godfrey Jr., M.D., commissioner.

4. Fellows, H. H.: J. Indust. Hyg. & Toxicol. **22**: 157 (May) 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

QUESTIONNAIRE FOR MEDICAL ENROLMENT

On this page appears a facsimile, greatly condensed, of a questionnaire which is now being sent to every licensed physician in the United States and in all its territories. This questionnaire is being sent at the request of the Surgeon Generals of the United States Army, Navy and Public Health Service as part of the plan for preparedness of the medical profession to enable our country to meet any emergency which may arise. The questionnaire was developed with the advice and assistance of the members of the Committee on Medical Preparedness and of the Surgeon Generals. Just as soon as these questionnaires are received in the headquarters office of the American Medical Association the information supplied will be transferred to cards in a punch card system, so that it will be possible by the use of the usual machines to make a selection of physicians capable of serving in various military, naval, industrial or civil capacities.

COMMITTEE ON MEDICAL PREPAREDNESS
AMERICAN MEDICAL ASSOCIATION
535 North Dearborn Street, Chicago, Illinois

PLEASE USE TYPEWRITER OR PRINT ANSWERS

Disregard All Figures. These Are for Use on Key Cards only. Indicate Answers in Squares Thus ☒

1-15. Name ..... Surname ..... 16. Given Names ..... 17. Middle Name

18-19. State ..... County ..... City .....

Street address .....

20. Race: White ☐ Negro ☐ Asiatic ☐ Indian ☐ 28. Sex: Male ☐ Female ☐ 29-30. Year of birth .....

31. Marital status: Single ☐ Married ☐ Widowed ☐ 32. Number of dependents: Under 10 years ..... Over 10 years .....

34. Citizenship: Native born ☐ Naturalized ☐ Non-citizen ☐ 35-36. Date and place of naturalization ..... Year ..... Place .....

37-38. Country of birth ..... 39. Language spoken: French ☐ German ☐ Spanish ☐ Italian ☐ Russian ☐ Swedish ☐ Portuguese ☐ Other ☐

40-41. Graduate of ..... Exact name of medical school or class of graduation

42-43. State in which school is located ..... 44-45. Year of graduation .....

46-47. First year of licensure ..... 48. Are you now a member of a county medical society? Yes ☐ No ☐

49. Are you a member of any hospital staff? Yes ☐ No ☐ Name of principal hospital .....

50. Do you hold any of the following appointments that require your full time? Yes ☐ No ☐

51. State health department ☐ Local health department ☐ Teaching ☐ Research ☐ Hospital administration ☐ Executive ☐ Industrial ☐ Veterans administration ☐ Indian Field Service ☐

52. Type of practice: General ☐ Special ☐ 53. If a specialist, do you hold a certificate from a special examining board? Yes ☐ No ☐

54-55. If yes, from which of the following special examining boards? American Board of Pediatrics ☐ Psychiatry and Neurology ☐ Orthopedic Surgery ☐ Dermatology and Syphilology ☐ Radiology ☐ Urology ☐ Obstetrics and Gynecology ☐ Internal Medicine ☐ Pathology ☐ Ophthalmology ☐ Otolaryngology ☐ Surgery ☐ Anesthesiology ☐ Plastic Surgery ☐

56-57. Year first certificate received .....

58. Are you a member of any special medical societies? Yes ☐ No ☐ 59. If so, indicate under the proper heading below, exact name of the two most important: Surgery, Gynecology, Obstetrics, Orthopedics, Proctology and Anesthesia .....

Ophthalmology, Otology, Laryngology and Rhinology .....

Dermatology and Urology .....

Pediatrics and Internal Medicine .....

Neurology and Psychiatry .....

Pathology, Bacteriology and Anatomy .....

Roentgenology and Radiology .....

If a specialist, place a cross (x) opposite the specialty to which you devote ALL of your time or a figure (1) to indicate the specialty to which you devote the major portion of your practice and a figure (2) to indicate the specialty which occupies the remainder of your time.

60. 1. Surgery ☐
61. 1 (a) Brain and Nerve ☐
2 (b) Plastic ☐
60. 2. Industrial Practice ☐
61. 1 (a) Surgery ☐
2 (b) Preventive ☐
3 (c) Consultation ☐
4 (d) Toxicology ☐
5 (e) Teaching ☐
60. 3. Obstetrics ☐
4. Gynecology ☐
5. Obstetrics and Gynecology ☐
6. Orthopedic Surgery ☐

62. 1. Proctology ☐
2. Urology ☐
3. Dermatology ☐
4. Ophthalmology ☐
5. Otology, Laryngology, Rhinology ☐
6. Ophthalmology, Otology, Laryngology, Rhinology ☐
7. Pediatrics ☐
8. Neurology ☐
9. Psychiatry ☐

63. 1. Neurology and Psychiatry ☐
2. Internal Medicine ☐
3. Tuberculosis ☐
4. Anesthesia ☐
5. Roentgenology, Radiology ☐
6. Pathology ☐
7. Clinical Pathology ☐
8. Bacteriology ☐
9. Public Health ☐

64. Activity and method of practice: Individual ☐ Partnership ☐ Group ☐ Salary ☐ Resident ☐ Other ☐ Retired ☐ Not in practice ☐

65. Previous military experience, 1917 to 1919. Army ☐ Navy ☐ 66. U. S. P. H. S. ☐ 66. In U. S. ☐ Abroad ☐ 67. Rank .....

68. Present commission held: Army ☐ Navy ☐ U. S. P. H. S. ☐ Army Reserve ☐ Naval Reserve ☐ National Guard ☐ 69. Rank .....

70-73. Date of present commission: Month ..... Year ..... 74. In the event of war will you volunteer for military service? Yes ☐ No ☐

75-76. Service you consider yourself best qualified to perform .....

77. Do you know of your own knowledge that you are unfit for military service? Yes ☐ No ☐

78. Reason for disability: Vision ☐ Hearing ☐ Crippling defects ☐ Other reasons for disability may be stated on reverse side.

PLEASE REREAD AND VERIFY YOUR ANSWERS
RETURN AT ONCE IN THE ENCLOSED SELF ADDRESSED ENVELOPE
Use Reverse Side for Remarks

The physician who receives this questionnaire should take the necessary time and give the necessary thought to supplying a complete and absolutely correct reply. It is the desire of the authorities, should an emergency arise, to place every individual capable of rendering aid in the position in which he can be of the utmost service, and also naturally where his training and his experience most definitely qualify him. It will be observed that opportunity is offered to state appointments in hospitals, together with the nature of the appointment, membership in special medical organizations, together with the nature of such membership, and whether or not the physician possesses the certificate of one of the examining boards in the medical specialties. There is also opportunity to provide complete information concerning the civil status of the physician concerned, whether or not he practices alone or in association with other physicians, whether or not he is married and has children, and whether or not he has any physical incapacity which might prevent him from doing certain types of service.

It is hoped that every physician will cooperate with the Committee on Medical Preparedness and with the United States government by filling out this blank and returning it at the earliest possible moment. Obviously, as physicians are needed, an attempt will be made to supply them through this mechanism. If conscription should become necessary, every effort will no doubt be made to assign physicians to work for which they are especially suited. Those who have failed to cooperate will naturally take the chance of being assigned to any kind of service which may offer, and perhaps with far less possibility of rendering the quality of aid they are capable of rendering. When Canadian physicians were requested to provide similar information more than 90 per cent volunteered to serve in any capacity to which they should be assigned. Our medical profession has always enrolled itself among the leaders in patriotism and love of our country.

Cooperation and preparedness at this time constitute the duty of every American citizen who enjoys his citizenship and wishes to preserve the American democracy.

COMMITTEE ON MEDICAL PREPAREDNESS

Dr. Irvin Abell, Louisville, Ky., Chairman
Dr. Charles A. Dukes, Oakland, Calif.
Dr. Roy W. Fouts, Omaha
Dr. Stanley H. Osborn, Hartford, Conn.
Dr. John H. O'Shea, Spokane, Wash.
Dr. James E. Paullin, Atlanta, Ga.
Dr. Walter G. Phippen, Salem, Mass.
Dr. Fred W. Rankin, Lexington, Ky.
Dr. Harvey B. Stone, Baltimore
Dr. Samuel E. Thompson, Kerryville, Texas

Ex Officio:
Dr. Arthur W. Booth, Elmira, N. Y., Chairman Board of Trustees
Dr. Austin A. Hayden, Chicago, Secretary Board of Trustees
Dr. Nathan B. Van Etten, New York, President American Medical Association
Dr. Olin West, Chicago, Secretary American Medical Association
Dr. Morris Fishbein, Chicago, Editor Journal of the American Medical Association

ORGANIZATION SECTION

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. R. 5874 has been reported to the House, proposing to include the name of Gustaf E. Lambert among those honored by an act recognizing the high public service rendered by Major Walter Reed and those associated with him in the discovery of the cause and means of transmission of yellow fever. The Senate rejected a proposed amendment to the Revenue Act of 1940 which would have exempted from the increased tax on distilled spirits all alcohol used exclusively for manufacturing drugs. Senator McKellar, Tennessee, in submitting this amendment stated that one of the principal ingredients in all "patent medicines" is alcohol and that "'patent medicines' are the poor man's doctor."

Bills Introduced.—S. 4179, introduced by Senator Walsh, Massachusetts, provides for the establishment of a National Physical Fitness Institute in the Federal Security Agency. The institute will be authorized, if the bill is enacted, to (1) select, prepare and conduct research with respect to tests and testing instruments for the purpose of testing physical fitness; (2) select, prepare and conduct research with respect to follow-up procedures, forms of reports, and methods of cooperating with agencies engaged in medical and health work, for the purpose of conserving and increasing the physical fitness of the American people; (3) conduct research for the purpose of determining the most efficient and practical methods of conserving and increasing physical fitness; (4) train specialists in the work of conserving and increasing physical fitness; (5) prepare reports and bulletins with respect to the conservation and increase of physical fitness for use by organizations and the general public; (6) on request, investigate the needs of organizations and industries for and, to the extent possible with its personnel, cooperate with such organizations and industries in providing physical fitness services for their members and employees, and (7) cooperate with departments and other agencies of the government in programs designed to conserve and increase the physical fitness of their officers and employees. H. R. 9951, introduced by Representative Edelstein, New York, proposes to provide workmen's compensation for employees of carriers engaged in interstate transportation by motor vehicles. The duty is to be devolved on the employer to furnish such medical, surgical and other attendance or treatment, nurse and hospital service, medicine, crutches and apparatus for such period as the nature of the injury of the employee or the process of recovery may require. All fees and other charges for such treatment or service will be limited to such charges as prevail in the same community for similar treatment of injured persons of like standard of living and will be subject to regulation by the deputy commissioner of the United States Employees' Compensation Commission having jurisdiction in respect of an injury.

OFFICIAL NOTES

ABSTRACT OF MINUTES OF MEETINGS OF BOARD OF TRUSTEES HELD IN NEW YORK CITY, JUNE 9-13, 1940

A full day meeting of the Board was held on Sunday, June 9, and meetings of shorter duration were held each day from Monday to Thursday inclusive of the week of the annual session. Some of the deliberations of the Board are reflected in the following actions. Other matters too numerous to mention were discussed.

NATIONAL PREPAREDNESS

A special committee appointed for the purpose brought in a resolution suggesting the creation of a Committee on National Preparedness, whose duty it would be to establish and maintain contact and suitable relationship with all governmental agencies concerned with the prevention of disease and the care of the sick, in both civil and military aspects, so as to make available at the earliest possible moment every facility that the American Medical Association can offer for the health and safety of the American people and for the maintenance of American democracy.

The Board approved the necessary expenditure for the compilation of information relative to the physicians of the country which can be made available to the government.

INDICTMENT OF ASSOCIATION

Dr. Olin West, Secretary and General Manager of the American Medical Association, was authorized to appear before the United States District Court for the District of Columbia on Friday, June 14, to enter a plea of not guilty for the Association in the case of the United States vs. the Medical Society of the District of Columbia, Harris County Medical Society, certain members of the Medical Society of the District of Columbia and certain members of the administrative personnel of the American Medical Association. Dr. Fishbein was authorized to enter the plea of not guilty in the event that Dr. West could not do so.

CHANGE IN NAME AND POLICIES OF COUNCIL ON FOODS

The Board approved the change in name of the Council on Foods to Council on Foods and Nutrition and a change in its policies so as to concentrate its efforts on the important function of expressing authoritative group opinion on foods and the nutritional claims made for them, and to avoid effort that would duplicate the activities of the Federal Food, Drug and Cosmetic Administration.

REPRESENTATIVES OF ASSOCIATION TO OTHER ORGANIZATIONS

Dr. Fishbein was appointed a member of the Committee on Education and the Committee on Publications of the National Foundation for Infantile Paralysis.

Dr. W. W. Bauer was authorized to continue to serve for another two years as a member of the General Advisory Committee on Maternal and Child Welfare Services to assist in the development of sound working relationships between the federal government and the states in the extension and improvement of health and welfare services for the mothers and children of the United States.

Mr. Howard A. Carter, Secretary of the Council on Physical Therapy of the American Medical Association, was appointed as alternate representative of the American Medical Association on the Committee on Acoustical Measurements and Terminology of the American Standards Association. Dr. Austin A. Hayden is the representative of the American Medical Association on that committee.

Dr. George M. Lyon, of Huntington, W. Va., was appointed to succeed Dr. Edward Jackson on the Joint Committee on Health Problems in Education of the American Medical Association and the National Education Association.

Dr. W. W. Bauer was appointed to serve as a member of the Year Book on Health Education for the American Association of School Administrators.

STANDARD CLASSIFIED NOMENCLATURE OF DISEASE

The following physicians were appointed to constitute the Editorial Advisory Board of the Standard Classified Nomenclature of Disease: Drs. George Baehr, Dana W. Atchley, Neil A. Dayton, Bowman C. Crowell, Christopher G. Parnall, Halbert S. Dunn and James R. Miller, with Dr. E. P. Jordan as Chief Editor.

ABSTRACT JOURNAL COVERING CLINICAL MEDICINE AND SURGERY

Further consideration of the publication of an abstract journal of clinical medicine and surgery by the Association was postponed for the reason that the publication of some foreign periodicals seems to have been suspended on account of the disturbing conditions abroad and that others are not being received at regular intervals.

RED CROSS SOCIETIES TO REPRODUCE ARTICLES FROM HYGEIA

Permission was granted to the League of Red Cross Societies, Geneva, Switzerland, to reproduce or summarize in their Red Cross magazines articles appearing in HYGEIA.

OFFICERS OF BOARD OF TRUSTEES FOR ENSUING YEAR

The following officers and committees were elected for the ensuing year: Chairman, Dr. Arthur W. Booth; Secretary, Dr. Austin A. Hayden; Executive and Finance Committee: Drs. Bloss, Sensenich and Hayden; Committee on Scientific Exhibits: Drs. Cullen, Henderson and Lee.

RESOLUTION IN HONOR OF DR. CHARLES B. WRIGHT

A resolution on the death of Dr. Charles B. Wright, who had been a member of the Board for seven years and who had served as Chairman of the Executive Committee for three years, was adopted for presentation to the House of Delegates.

WOMAN'S AUXILIARY

Arkansas

Dr. T. P. Foltz spoke on "Should Medicine Be Socialized on a National Scale?" at a joint meeting of the auxiliary to the Sebastian County Medical Society and the Parent-Teacher Association in Fort Smith, March 7.

At an open meeting arranged by the auxiliary to the Pulaski County Medical Society at the University of Arkansas School of Medicine, Little Rock, February 21, Dr. A. S. Buchanan, president of the Arkansas Medical Society, spoke on socialized medicine and Mrs. C. E. Kitchens, president of the auxiliary, spoke on the life of Jane Todd Crawford.

California

One hundred and seventy-nine members and guests attended the regular meeting of the auxiliary to the Los Angeles County Medical Association in Long Beach, February 27. Capt. Joel T. Boone, U. S. Navy, was the speaker.

Mr. F. J. O'Ferrall, Chief Inspector of the State Division of Narcotic Enforcement, addressed the auxiliary to the Fresno County Medical Society, February 6.

At a meeting of the auxiliary to the Marin County Medical Society held in Fairfax, February 22, Mr. Robin Lampson summarized his book, "Death Loses a Pair of Wings," a story of the life of Dr. William C. Gorgas.

Mrs. Julian Jacobson reviewed "Life and Death: The Autobiography of a Surgeon," by Andrea Majocchi, at a meeting of the auxiliary to the Santa Cruz County Medical Society, February 26.

District of Columbia

The auxiliary to the Medical Society of the District of Columbia held its annual reception in Washington, January 23, under the presidency of Mrs. Robert M. Bolton. Mrs. V. E. Holcombe, president-elect of the auxiliary to the American Medical Association, was guest of honor.

The auxiliary has helped the Red Cross by copying braille manuscripts and by making surgical dressings for patients. It has raised money for the Orthopedic Clinic of the Children's Hospital and for the "Incubator Fund," the purpose of which is to place incubators in all the hospitals in the District of Columbia. The auxiliary has contributed clothing and household goods to the Self-Help Exchange, toys and gifts to children at the Heart Clinic and a radio to the Children's Hospital.

Illinois

At the March meeting of the auxiliary to the Chicago Medical Society Mrs. Jesse R. Gerstley talked on "Recent Escape Literature." At a meeting of the auxiliary, April 3, Dr. Rollo K. Packard spoke on "Hospital Facilities and Needs in the United States." Special guests were Mrs. Rollo K. Packard, president, auxiliary to the American Medical Association, Mrs. Eben J. Carey, chairman, *Hygeia* committee, auxiliary to the American Medical Association, and Mrs. Oscar W. Friske, past president, auxiliary to the State Medical Society of Wisconsin. At a meeting of the North Shore Branch of the auxiliary to the Chicago Medical Society on April 1 Dr. C. J. Barborka was speaker.——Mrs. Olive Bruner, principal of the Spalding School for Crippled Children, spoke on the subject "The Crippled Child in School" at the March meeting of the auxiliary to the Irving Park Branch of the Chicago Medical Society.——Mrs. Bernice Vandervries, representative, Sixth Congressional District of Illinois, discussed the duties of a representative and the importance of voting at the March meeting of the auxiliary to the Aux Plaines Branch of the Chicago Medical Society.

Mrs. Charles C. Winning, president, auxiliary to the Illinois State Medical Society, discussed the aims of the auxiliary at the charter meeting of the auxiliary to the Peoria County Medical Society, March 5. Fifty-seven women signed the charter of the newly formed auxiliary. At the following meeting, April 2, members discussed the Wagner Health Bill.

Dr. Elizabeth Ball, Department of Public Health, State of Illinois, discussed "Health, Weight and Diet" at a public relations meeting of the auxiliary to the Knox County Medical Society in Galesburg, March 22.

The county health program was discussed at a meeting of the auxiliary to the Adams County Medical Society in Quincy, March 11. Dr. James H. Hutton, president of the Illinois State Medical Society, spoke on "Some Important Facts All Auxiliary Members Must Know" at a meeting of the auxiliary in Quincy, April 8.

Indiana

Thomas A. Hendricks, executive secretary, Indiana State Medical Association, spoke on socialized medicine before the auxiliary to the Tippecanoe County Medical Society, Lafayette, March 12.

Kansas

The auxiliary to the Labette County Medical Society met in Parsons, January 24. A paper on the life of Florence Nightingale was read by one of the members.

The auxiliary to the Wyandotte County Medical Society met in Kansas City, January 12. Miss Viola Garret gave an account of her vacation trip through the Scandinavian countries.

Oklahoma

The auxiliary to the Le Flore County Medical Society sponsored programs on socialized medicine for the Parent-Teacher Association with addresses by Dr. Rush Wright and Mrs. Loton Shippey, president of the auxiliary, in Poteau recently. In February, the auxiliary and the Federation of Women's Clubs held a joint meeting for the public on cancer control in Poteau, at which time Dr. J. S. Binkley, of New York, was the speaker.

The auxiliary to the Tulsa County Medical Society placed *Hygeia* in all the public schools of Tulsa County. The auxiliary purchased a new short wave diathermy apparatus for the Tulsa County Medical Clinic recently and has made and distributed a large number of garments for infants.

The auxiliary to the Pottawatomie County Medical Society placed copies of *Hygeia* in all rural communities adjacent to Shawnee.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

State Medical Election.—Dr. Samuel A. Gordon, Marion, was elected president of the Medical Association of the State of Alabama at its recent annual meeting. Drs. Merle E. Smith, Parrish, and Douglas L. Cannon, Montgomery, were reelected vice president and secretary-treasurer, respectively. Mobile was selected for the next annual session, April 15-17, 1941.

CALIFORNIA

Restriction of Sale of "Sleeping Potions."—To reduce the death toll from drugs heretofore purchased without restrictions, the state board of pharmacy adopted a resolution prohibiting the sale of dangerous sleeping potions, according to the Los Angeles *Times*. Since January 1 there have been twenty-three deaths in Los Angeles and vicinity and seven in the San Francisco area, either through suicide or accident, as a result of promiscuous purchase of deadly drugs, it was stated. The state department of public health took similar action, May 25, its resolution naming as dangerously poisonous drugs, chemicals and medicinal substances the following: veronal, barbital, acid diethylbarbituric, barbituric acid, or any of their salts, derivatives or compounds, phenobarbital, or any of its salts or compounds, acetylurea, sulfonated methanes, or any of their salts, derivatives or compounds. Once filled, prescriptions are not to be refilled without the written order of the prescriber, it was reported.

Housman Sentenced.—Dr. Nathan S. Housman, San Francisco, was sentenced to San Quentin prison, June 13, to a term of from one to fourteen years, after the court had denied a motion for a new trial. Housman was indicted by the grand jury, November 1, on six counts: two of perjury, two of preparing false evidence and two of offering false evidence. Shortly before his indictment, Dr. Housman had been acquitted in municipal court on two misdemeanor charges involving narcotic prescriptions, according to the state board of medical examiners. It was stated that testimony was given to prove that Dr. Housman perjured himself at the jury trial prior to the indictment when he said that he kept case records showing narcotic prescriptions issued to patients. Material from the state board of medical examiners states that the falsification charges were based on an allegation that Dr. Housman's case records showing narcotic prescriptions had been copied after the start of his trial from records of prescriptions kept at the drugstore at which the prescriptions were filled. Judge Lile T. Jacks imposed the sentence of from one to fourteen years on each of the two counts of perjury and of from one to five years on each of the other counts, all of the terms to run concurrently. Dr. Housman graduated at Jefferson Medical College of Philadelphia in 1922.

CONNECTICUT

Changes in Health Officers.—Dr. Howard S. Allen, Woodbury, has been appointed health officer of Bethlehem; Dr. Morton H. Chapnick of the town of Putnam and city of Putnam, and Dr. Francis Brae Rafferty, Willimantic, of Lebanon.

State Medical Election.—Dr. James D. Gold, Bridgeport, was named president-elect of the Connecticut State Medical Society at its annual meeting in Hartford, May 21, and Dr. Arthur B. Landry, Hartford, was inducted into the presidency. Dr. Creighton Barker, New Haven, was reelected secretary. The next annual session will be in Bridgeport, May 20-22, 1941.

Appointments at Yale.—Dr. John R. Paul and Leon S. Stone, Ph.D., both associate professors, have been appointed professor of preventive medicine and Bronson professor of comparative anatomy respectively at Yale University School of Medicine, New Haven. Dr. Paul graduated at Johns Hopkins University School of Medicine, Baltimore, in 1919 and has been on the Yale faculty since 1926. Dr. Stone received his doctorate at Yale in 1921. George H. Smith, Sc.D., professor of immunology, has been appointed assistant dean for the next college year.

IDAHO

Society News.—The South Side Medical Society was addressed in Twin Falls, May 17, by Drs. Fern M. Cole, Caldwell, president of the state medical association, who discussed the value of medical organization, and Casper W. Pond, Pocatello, deep infections of the neck.

Study of Silicosis.—A mobile x-ray unit, built by the state industrial accident board and state division of public health, is making a tour of the state under the direction of the bureau of industrial hygiene. All industrial workers exposed to silica dust will be examined. According to *Northwest Medicine*, the information will be used for statistical purposes only and it is not expected that the unit will be used to replace any existing medical service.

INDIANA

Course in Obstetrics.—The St. Joseph County Medical Society and the bureau of maternal and child health of the Indiana State Board of Health conducted a postgraduate course in obstetrics in South Bend, June 3-5. Sessions were held at Epworth and St. Joseph hospitals. The course was under the direction of Dr. Carl P. Huber, assistant professor of obstetrics, Indiana University School of Medicine, Indianapolis, and director of postgraduate education in obstetrics of the state board of health.

New Hospital Library.—The new $8,000 library at the Indianapolis City Hospital was dedicated May 14. It was the gift of Eli Lilly & Co. A feature of the dedicatory program was the presentation of the first volume to the library by Dr. William N. Wishard Sr., superintendent of the hospital from 1879 to 1887. The book was the "Autobiography of Dr. Harvey Wiley." Dr. Wishard also presented photographs of Dr. Wiley and of Dr. Livingston Dunlap to the library. The latter is credited with founding the hospital. Dr. Charles W. Myers, now superintendent of the city hospital, presided at the dedicatory ceremonies.

Direction of Medical Schools Consolidated.—Dr. Willis D. Gatch, dean and professor of surgery, Indiana University School of Medicine, Indianapolis, has been appointed to direct the unit at Bloomington, newspapers announced June 22. In the latter capacity he succeeds Dr. Burton D. Myers, whose retirement was announced in THE JOURNAL, June 15. According to the report, the consolidation of direction will assure continuity of training at minimum cost and maximum effectiveness for students. Jacob A. Badertscher, Ph.D., professor of anatomy at Bloomington since 1921, will be assistant to Dr. Gatch in Indianapolis, and Dr. Edwin N. Kime, who has been a member of the faculty since his graduation from the school in 1916, will be in charge of the department of anatomy on both campuses, giving full time to the work. Dr. Badertscher holds Ph.D. degrees from Ohio and Cornell universities and the degree of Ph.M. from Ohio University, Athens, Ohio. After serving on the faculties of both of these schools he joined the Indiana faculty in 1914. Dr. Gatch has been professor of surgery at the university since 1911 and dean since 1931.

IOWA

State Medical Election.—Dr. Earl B. Bush, Ames, was chosen president-elect of the Iowa State Medical Society at its annual session in Des Moines, May 3, and Dr. Frank P. McNamara, Dubuque, was inducted into the presidency. Dr. Robert L. Parker, Des Moines, was reelected secretary. Davenport was designated as the place for the next annual session, May 14-16, 1941.

Society News.—Dr. Norbert C. Barwasser, Davenport, addressed the Muscatine County Medical Society, May 23, on "Management of the Commoner Skin Diseases."——Dr. Palmer Findley, Omaha, discussed "Socialized Medicine in Sweden" before the Des Moines Academy of Medicine and the Polk County Medical Society recently.——Dr. William D. Paul, Iowa City, discussed "Recent Advances in Hypertension" at a meeting of the Bremer County Medical Society and the staff of Mercy Hospital in Waverly recently.——The Hardin County Medical Society was addressed in Iowa Falls recently by Dr. Joseph B. Priestley, Des Moines, on "Nonsurgical Management of Gallbladder Disease."——Dr. Willard O. Thompson, Chicago, discussed "Treatment of Hypogonadism Pertinent to Endocrinology" before the Woodbury County Medical Society recently.——Dr. Elmer E. Kottke, Des Moines, addressed the Hancock-Winnebago County Medical Society recently on "Heart Disease and Coronary Hypertension."

KANSAS

State Medical Election.—Dr. Clyde D. Blake, Hays, was chosen president-elect of the Kansas Medical Society at its recent annual meeting in Wichita and Dr. Forrest L. Loveland, Topeka, was installed as president. Dr. John M. Porter, Concordia, is secretary, and Mr. Clarence G. Munns, Topeka, executive secretary. Topeka was selected as the place for the 1941 session.

MASSACHUSETTS

Conference on Tomorrow's Children.—The Harvard Summer School and the National Conference on Family Relations will sponsor a New England Conference on Tomorrow's Children at Littauer Center, Harvard University, Cambridge, July 24-26. The conference program will consist of panel and round table discussions. Among physicians who will take part at various times are:

Dr. John Rock, research associate in obstetrics and instructor of gynecology, Harvard Medical School, Boston.
Dr. Merrill Moore, associate in psychiatry, Harvard Medical School, Boston.
Dr. Florence Clothier, psychiatrist, New England Home for Little Wanderers, Boston.
Dr. James C. Janney, assistant professor of gynecology, Boston University School of Medicine.
Dr. Woodbridge E. Morris, New York, medical director, Birth Control Federation of America.
Dr. Anna L. Philbrook, New Hampshire State Hospital, Concord.
Dr. George Gilbert Smith, Boston, president, Massachusetts Society for Social Hygiene.
Dr. Regine J. K. Stix, Milbank Memorial Fund, New York.
Dr. Eric P. Stone, Providence, R. I., chairman, medical advisory board, Rhode Island Maternal Health Association.

New Society for Research in Psychiatry.—The Massachusetts Society for Research in Psychiatry was organized at a meeting, May 2, to stimulate research in psychiatric medicine and the sciences allied to it in the psychiatric institutions of the state. The active membership is limited to those who have completed or presented before a recognized scientific society, or published in a recognized scientific journal, results of research work which they have done within the last five years. This active membership will cease after more than three years has elapsed without production of original work, the member becoming an associate member. The associate members are selected from those having a satisfactory background and training which will render them suitably qualified to become research workers and from those who are participating in research work. Meetings will be held six times a year at the various hospitals engaged in neuropsychiatric work. They are to be devoted to symposiums and to informal discussions of projects, methods, technics and demonstrations of research work actively engaged in or under consideration. Officers of the new society include Drs. William Malamud, Worcester, president; Paul I. Yakovlev, Waltham, vice president, and Kenneth J. Tillotson, Belmont, secretary-treasurer.

MICHIGAN

Personal.—Dr. Harry H. Haight, Crystal Falls, has been appointed superintendent of the Penn Iron Mining Company Hospital, Norway, to succeed Dr. Lloyd E. Hamlin, who resigned to become medical director of the plant of the Bethlehem Steel Corporation, Bethlehem, Pa., newspapers reported. ——Dr. Charles M. Turrell, physician to the Detroit police department since 1914, has retired.——Dr. Frank H. Power, Ann Arbor, has been appointed by the governor as cancer consultant to the state department of health; in this capacity he will serve as field agent for the department and the cancer committee of the Michigan State Medical Society and will be available as a consultant to practicing physicians. He succeeds Dr. Clifford H. Keene, who resigned.——Dr. Stuart Pritchard, president and general director of the W. K. Kellogg Memorial Foundation, Battle Creek, received the honorary degree of doctor of science from the University of Michigan, Ann Arbor, June 15, for "distinguished and outstanding contributions to the field of medicine and public health."

MISSISSIPPI

State Medical Election and Meeting.—Dr. Augustus Street, Vicksburg, was named president-elect of the Mississippi State Medical Association at its seventy-third annual meeting in Jackson, May 16, and Dr. William H. Anderson, Booneville, was installed as president. Other officers are Drs. Charles E. Mullins, Bude; Martin L. Flynt Sr., Meridian, and William H. Curry, Eupora, vice presidents. Dr. Thomas M. Dye, Clarksdale, was reelected secretary. The 1941 session will be held in Biloxi, May 13-15. Dr. Irvin Abell, Louisville, Ky., gave the Ewing Howard Fox Oration on "Some Contributions of the Profession to the Public." Included among other speakers were:

Dr. Edgar W. Davis, Washington, D. C., Lobectomy and Pneumonectomy in Nontuberculous Disease of the Lungs.
Dr. Edward C. Ellett, Memphis, Tenn., Some Points in Eye Surgery.
Dr. Alston Callahan, Vicksburg, Tumors of the Orbit.
Dr. John J. Shea, Memphis, Tenn., Frequent Errors in Tonsil and Adenoid Surgery.
Dr. William Lauch Hughes, Jackson, Diseases of the Nasopharynx.
Dr. Fred Geisenberger, Natchez, Modified Barraquer Suction Extraction of Cataracts.
Dr. Douglas D. Baugh, Columbus, Intercepting Cancer in the Female Reproductive Organs.
Dr. Robert Lyle Motley, Memphis, Tenn., Some Points in the Diagnosis and Treatment of Indigestion.
Dr. Charles E. Ward, Jackson, Treatment of Eczema in Children.
Dr. John G. Archer, Greenville, Some Observations of Bundle Branch Block.
Dr. Rudolph H. Kampmeier, Nashville, Tenn., Benign Tertiary Manifestations of Syphilis Presenting Difficulties in Diagnosis.
Dr. Aubrey V. Beacham, Magnolia, Systemic Effects of Frequently Overlooked Urinary Diseases.
Dr. Willard H. Parsons, Vicksburg, Indications for and Results from Operations on the Biliary Tract.
Dr. John C. Henthorne, Jackson, Pathologic Defections of the Corpus Luteum of the Ovary.
Dr. Hugh A. Gamble, Greenville, Breast Cancer, Its Treatment and the Cautery Technic of Operation.
Dr. Van Buren Philpot, Houston, Cesarean Section.

One of the features of the meeting was the presentation of a portrait of Dr. John Wesley Monette, 1803-1851, for Mississippi's first medical hall of fame. The presentation was made by Judge Gerald Brandon, Natchez, grandson of Dr. Monette.

NEW MEXICO

State Medical Election.—Dr. Carl Mulky, Albuquerque, was chosen president-elect of the New Mexico Medical Society at its fifty-eighth annual meeting and Dr. William B. Cantrell, Gallup, was installed as president. Drs. Wallace P. Martin, Clovis, and Leo B. Cohenour, Albuquerque, were reelected vice president and secretary-treasurer, respectively. Raton was selected as the place for the 1941 annual meeting.

NEW YORK

Personal.—The Delaware County Medical Society gave a reception May 21 to honor Dr. Robert Brittain, Downsville, on his completion of fifty years of medical practice.——Dr. John H. Korns, Olean, who has resigned as superintendent of Rocky Crest Sanatorium and director of tuberculosis work of Cattaraugus County, was honored with a testimonial dinner before his departure for Westchester County. About 200 friends of Dr. and Mrs. Korns attended and Dr. Theodore J. Holmlund, Cattaraugus, president of the Cattaraugus County Medical Society, presented them with a silver bowl, the gift of friends throughout the county. Dr. Korns became director of the division of tuberculosis in the Westchester County health department May 16.

Syracuse Alumni Meeting.—The medical alumni of Syracuse University School of Medicine, Syracuse, held a meeting in connection with commencement June 3-4. Dr. George H. Whipple, Rochester, was the guest speaker at an afternoon session on "Protein Construction and Exchange in the Body—Including Hemoglobin and Plasma Proteins," followed by section meetings on surgery, medicine, pediatrics and gynecology and obstetrics. Tuesday morning addresses were made by Drs. Jesse G. Marthens, Dayton, Ohio, and Leonard K. Stalker, Rochester, Minn., whose subjects were: "Can We Eliminate the Shadow on the Land?" and "Management of Acute Conditions Within the Abdomen" respectively. Dr. George Baehr, New York, was the guest speaker at the annual banquet Monday evening at the Onondaga Hotel.

New York City

Medal Awarded to Dr. Greene.—Dr. James Sonnett Greene, founder and director of the National Hospital for Speech Disorders, was awarded a medal by the American Laryngological, Rhinological and Otological Society at its meeting in New York, June 7, "for his unselfish devotion to the alleviation of speech defects in those thus afflicted, and for the success which has crowned his lifelong efforts in having established the National Hospital for Speech Disorders." A citation accompanied the medal, which is said to be the fourth awarded by the association in the forty-six years of its existence. Dr. Greene graduated at Cornell University Medical College, New York, in 1902.

Health and Teaching Centers Completed.—The Washington Heights Health and Teaching Center, last of a group of centers affiliated with the five medical schools in New York, was dedicated June 10. The new center adjoins the College

of Physicians and Surgeons of Columbia University, with which it is associated, on land made available by the Presbyterian Hospital. Mayor La Guardia made the principal address and other speakers included Drs. Nathan B. Van Etten, President of the American Medical Association; Willard C. Rappleye, dean and professor of medical economics of the College of Physicians and Surgeons, and John L. Rice, commissioner of health. The Lower East Side Health and Teaching Center, 341 East Twenty-Fifth Street, affiliated with New York University College of Medicine, was dedicated, May 15. The speakers included the mayor, Dr. Rice, Harry Woodburn Chase, LL.D., chancellor of New York University, which donated the land for the building; Dr. Currier McEwen, dean and associate professor of medicine, of New York University College of Medicine; Dr. Harry S. Mustard, Hermann M. Biggs professor of preventive medicine at the college, and John M. Schiff, president of the Henry Street Settlement, which will provide nursing services at the center. The new structure, adjoining the college of medicine, cost about $375,000. Child health and dental clinics are on the first floor; tuberculosis and rheumatic cardiac services on the second; offices for health education and the Henry Street Visiting Nurse Service on the third floor; quarters for the district health officer and his staff on the fourth, and class rooms and laboratories of the department of preventive medicine of the college of medicine on the fifth and sixth floors. This teaching center is the fourth of the units the city has set up in cooperation with medical schools. Those opened previously are the Kips Bay-Yorkville center in cooperation with New York Hospital-Cornell University Medical College; East Harlem in cooperation with New York Medical College and Flower Hospital, and Red Hook-Gowanus in cooperation with Long Island College of Medicine.

NORTH CAROLINA

Dr. MacNider Resigns as Dean.—Dr. William deB. MacNider, dean of the University of North Carolina School of Medicine, Chapel Hill, since 1937, has resigned to continue his research activities as Kenan research professor of pharmacology. Dr. Walter Reece Berryhill, who has been assistant dean since 1937, has been made acting dean. Dr. MacNider graduated from the medical school of the university in 1903, became Kenan professor of pharmacology in 1905 and research professor in 1920.

Society Honors High Point Physician.—The Guilford County Medical Society gave a dinner recently in honor of Dr. David A. Stanton, High Point, who has practiced medicine for fifty-three years. Dr. Frederick R. Taylor paid tribute to Dr. Stanton as a physician and Mayor O. A. Kirkman lauded him as a citizen. The society presented to him an engraved scroll. Dr. Stanton graduated from Vanderbilt University School of Medicine, Nashville, in 1887 and has practiced in High Point since 1891. He has been mayor and health officer of the town, a member of the city council and of the board of education.

OKLAHOMA

Course in Obstetrics.—A new intramural postgraduate course for physicians in obstetrics and allied subjects was begun early in June under the auspices of the University of Oklahoma School of Medicine, Oklahoma City, in cooperation with the state department of health and the Children's Bureau of the U. S. Department of Labor, Washington, D. C. The course will be repeated intermittently as circumstances and demand may justify. In conjunction with the physicians' course, and with the same sponsor and cooperating agencies, the University of Oklahoma School of Nursing will offer a four month postgraduate course in obstetrics and related subjects.

Society News.—Dr. Tazwell D. Rowland, Shawnee, addressed the Pottawatomie County Medical Society, Shawnee, June 15, on "Mental Problems Met in General Practice."——The medical societies of Garfield, Kay, Noble, Payne and Pawnee counties held a joint meeting in Perry, June 20, with recreation in the afternoon and addresses in the evening by Dr. Henry H. Turner, Oklahoma City, president of the Oklahoma State Medical Association, on the problems of the association and Mr. Joseph Hamilton, executive secretary of the crippled children's commission, on phases of that work.——Dr. Forrest P. Baker, Talihina, addressed the Tulsa County Medical Society, Tulsa, May 27, on "Tuberculosis and Admissions to the State Hospital."

PENNSYLVANIA

District Meetings.—The Ninth Councilor District of the Medical Society of the State of Pennsylvania held a meeting in Punxsutawney, June 21. On the scientific program Dr. George E. Simpson, Indiana, presented a paper entitled "Stop and Go in Biliary Surgery"; Dr. Talcott Wainwright, Oil City, "Shock," and Dr. Frank A. Lorenzo, Punxsutawney, "A Message from the Committee on Industrial Health of the Medical Society of the State of Pennsylvania." Dr. Francis F. Borzell, Philadelphia, president-elect of the state society, discussed activities of the society and a fifty year certificate was presented to Dr. Thomas N. McKee, Kittanning.——Drs. Edward F. Burt and David W. Kramer, Philadelphia, addressed the Fourth Councilor District meeting at Berwick, June 20, on "Respiratory Infections of Children" and "Progress Report on Control of Diabetes" respectively. Drs. Charles H. Henninger, Pittsburgh, president, and Walter F. Donaldson, Pittsburgh, secretary of the state society, made addresses and a fifty year testimonial certificate was presented to Dr. John W. Bruner, Bloomsburg.

Pittsburgh

Syphilis Control.—A program for the control of syphilis was inaugurated in Pittsburgh June 12 under grants from the city, the state, the federal government and the Buhl Foundation, amounting to $100,000. A general diagnostic clinic, to be coordinated with existing clinics, was opened at the Falk Clinic at the University of Pittsburgh, with Dr. William H. Guy as chief clinician, Dr. William W. Wightman as assistant chief clinician and twenty other physicians as part time clinicians. Six full time nurses are employed by the program and will be available to physicians for follow-up work. Dr. Albert E. Russell of the U. S. Public Health Service is temporary director of the program until it is under way, according to the Pittsburgh *Medical Bulletin*. Indigent patients will be treated at the clinics, but those able to pay will be referred to private physicians.

TEXAS

Special Society Elections.—Dr. Boen Swinny, San Antonio, was elected president of the Texas Allergy Association at its annual meeting, May 13, in Dallas, and Dr. Homer E. Prince, Houston, secretary.——Officers of the Texas Dermatological Society elected at the annual meeting, May 13, were Drs. William A. Smith, Beaumont, president; James Lewis Pipkin, San Antonio, vice president, and Duncan O. Poth, San Antonio, secretary.——Dr. William B. Carrell, Dallas, was made president of the Texas Orthopedic Association at its meeting, May 13; Dr. Edmund M. Cowart, Houston, vice president, and Dr. Mary Ruth Jackson, Dallas, secretary.——At the third annual meeting of the Texas Society of Gastro-Enterologists and Proctologists, May 13, officers elected were Drs. Milford O. Rouse, Dallas, president; Hugh C. Welsh, Houston, and Gilbert E. Brereton, Dallas, and Thomas E. Smith, Dallas, secretary.——Officers elected at the meeting of the Texas Association of Medical Anesthetists were Drs. Thomas H. Compere, Houston, president; Frank O. Barrett, El Paso, vice president, and Robert A. Miller, San Antonio, secretary.

VIRGINIA

Society News.—Dr. Ben M. Baker Jr., Baltimore, was the guest speaker at the annual all day clinic meeting of the Norfolk County Medical Society, Norfolk, recently on "The Therapeutic Use of Histamine." Clinics were held in the morning at the Norfolk General Hospital. Drs. Richard B. Nicholls and Charles J. Andrews addressed the society recently on "Obstetric Complications and Sterility" and "Management of the Third Stage of Labor, with Description of a New Technic for Delivery of the Placenta" respectively.——Drs. Byrd S. Leavell, Charlottesville, and William P. McGuire, Winchester, addressed the Medical Society of Northern Virginia in Winchester recently on "Acute Glomerulonephritis, Clinical Course and Treatment" and "Acute Oculoglandular Tularemia" respectively.——Theodore Blum, D.D.S., New York, addressed the annual joint meeting of the Peninsula Dental Society and the Warwick County Medical Association, recently in Newport on "Mouth Lesions: Their Diagnosis and Treatment."

Retires from State Service.—Dr. Bathurst B. Bagby, for several years director of the state bureau of child health, was to retire from service, July 1, newspapers reported. Dr. Bagby graduated at George Washington University School of Medicine, Washington, D. C., in 1904. He engaged in private prac-

tice until 1923, when he became health officer of Henrico County. In the following year he took a similar position in Clark County, Ga. He was health officer of Southampton County from 1929 to 1930, when he joined the staff of the state department of health. He was president of the Virginia Public Health Association in 1930.

WASHINGTON

Society News.—Dr. Wallace D. Hunt, Seattle, was elected president of the Washington Public Health Association at the annual meeting in Port Angeles, May 17-18.——Drs. Paul G. Flothow and Thomas W. Blake, Seattle, addressed the Cowlitz County Medical Society, Longview, May 15, on "Surgical Lesions of the Spine Causing Low Back Pain" and "Radiologic Aspects of Low Back Pain" respectively.——Dr. Alfred O. Adams, Spokane, addressed the Walla Walla Valley Medical Society, Walla Walla, May 9, on "Vitallium for Internal Fixation of Fractures."——Drs. Ross D. Wright and Charles P. Larson, Tacoma, addressed the Yakima County Medical Society, Yakima, May 13, on "Proctologic Surgery" and "Newer Knowledge of Vitamin K" respectively.

WEST VIRGINIA

Joint Meeting of State Societies.—The Medical Society of Virginia will hold its annual meeting jointly with the West Virginia State Medical Association, July 29-31, at the Greenbrier, White Sulphur Springs. General sessions will be held each morning and round table discussions each afternoon. The guest speakers will be:

Dr. Ralph M. Tyson, Philadelphia, Management of Urinary Infections in Childhood.
Dr. George E. Bennett, Baltimore, Orthopedic Treatment of Arthritis.
Dr. Carl M. Peterson, Chicago, The A. M. A. Bureau of Industrial Health.
Dr. Ross Golden, New York, Lesions of the Small Bowel.
Dr. Walter C. Alvarez, Rochester, Minn., The Patient Who Is Always Complaining.
Dr. Wesley C. Bowers, New York, Sinus Therapy.
Dr. Alfred I. Folsom, Dallas, Texas, The Female Bladder.
Dr. Harvey B. Stone, Baltimore, The Delayed Treatment of Appendicitis.
Dr. Karl M. Bowman, New York, Treatment of Delirium.
Dr. Frederick C. Irving, Boston, Treatment of Pernicious Vomiting.

Dr. Irvin Abell, Louisville, Ky., will deliver the oration on surgery and Dr. Paul Dudley White, Boston, the oration on medicine. Dr. Frank V. Langfitt, Clarksburg, president of the West Virginia association, and Dr. Hugh H. Trout, Roanoke, president of the Medical Society of Virginia, will deliver their official addresses Tuesday evening, July 30.

PUERTO RICO

Personal.—Dr. Cesar Dominguez, Humacao, has been reappointed a member of the Board of Medical Examiners of Puerto Rico.——Dr. Oscar G. Costa-Mandry, San Juan, president of the Puerto Rico Medical Association, has been made an honorary member of the Society of Physicians and Surgeons of Costa Rica.

GENERAL

Base Hospital Reunions.—The U. S. A. Base Hospital Camp Grant Reunion Association announces its annual reunion to be held in Milwaukee at the Y. M. C. A., Monday, September 16. Former medical officers, nurses and enlisted men of the Camp Grant Hospital are invited to attend this reunion. Reservations should be sent to Harold E. Giroux, president of the association, 841 Barry Avenue, Chicago.——Physicians who served at U. S. A. Base Hospital, Camp Sevier, Greenville, S. C., are requested to communicate with M. R. Callaway, 405 West Fourth Street, Dayton, Ohio, with regard to a reunion to be held in connection with the American Legion Convention in Boston, September 23-26.

Second Evaluation of Serologic Tests.—The Committee on Evaluation of Serodiagnostic Tests for Syphilis, in cooperation with the U. S. Public Health Service, is planning a study of serologic tests for syphilis or modifications of these within the next year similar to one conducted by the same committee in 1935. The methods used will be comparable to those used in the earlier study (THE JOURNAL, Dec. 1, 1934, p. 1705). If the need for an investigation of this kind seems to justify the cost, invitations will be extended to the authors of such serologic tests who live in the United States or who may be able to participate by the designation of a serologist who will represent them in this country. Serologists who have an original serologic test for syphilis or an original modification thereof and who desire to participate in the second evaluation study should submit their applications not later than October 1. The applications must be accompanied by a complete description of the technic of the author's serologic test or modification. All correspondence should be directed to the Surgeon General, U. S. Public Health Service, Washington, D. C.

National Board Celebrates Anniversary.—The National Board of Medical Examiners celebrated the twenty-fifth anniversary of its founding at a dinner at the Waldorf-Astoria, New York, June 12. Major-Gen. Merritte W. Ireland, president of the board, presided at the dinner and the speakers were Dr. Alan Gregg, director of medical sciences, Rockefeller Foundation, "A Sponsor's Greeting"; the Rev. Alphonse M. Schwitalla, Ph.D., dean, St. Louis University School of Medicine, "The Medical Schools"; Dr. Robert W. Keeton, professor of medicine, University of Illinois College of Medicine, "The Diplomates and the Medical Profession," and Dr. Walter L. Bierring, Des Moines, Iowa, "The First Twenty-Five Years." The board, founded in 1915 by Dr. William L. Rodman, Philadelphia, has received support from six foundations: Carnegie Foundation for the Advancement of Teaching, Rockefeller Foundation, Commonwealth Fund, Milbank Memorial Fund, General Education Board and the Carnegie Corporation. Its certificate is now accepted by forty-three states, the territories of the United States and several foreign countries. It now has thirty-two members.

Physician's Kit and Instruments Found.—In reporting the apprehension of one Woodfin Holsapple as an illegal practitioner in Illinois, the assistant state's attorney at Rock Island announces the finding of a physician's kit and instruments. The bag, which was in Holsapple's possession when he was arrested, contained the prescription book of a physician in Colorado, who has since reported that the kit and instruments are not his. No details were reported concerning Holsapple's activities in Illinois, but the assistant state's attorney suggested that some effort be made to return the apparently new kit to its rightful owner. It is suggested that any physician who has lost a kit or instruments should write Mr. Sam M. Arndt, assistant state's attorney, Rock Island, Ill., giving a description of the missing articles. Whether or not the Holsapple mentioned above is the same person as Woodfin Holesapple who was found to be posing as a physician in Colorado in 1939 is not known. Subsequent investigation disclosed that the latter individual had never obtained a medical degree from any university and that he had never practiced (legally) medicine. The person in this case pleaded guilty and was sentenced to serve six months in the Denver County jail.

Special Society Elections.—Dr. Andrew C. Ivy, Chicago, was elected president of the American Gastro-Enterological Association at the annual meeting in Atlantic City, N. J., in June. Drs. Russell S. Boles, Philadelphia, and Sara M. Jordan, Boston, were elected vice presidents and Dr. Thomas T. Mackie, New York, was made secretary. The 1941 meeting will be held in Atlantic City at the Hotel Claridge, May 5-6.——Dr. Fred O. Butler, Eldridge, Calif., was chosen president-elect of the American Association on Mental Deficiency at its annual session in May and Meta L. Anderson Post, Ph.D., Newark, N. J., was inducted into the presidency. Dr. E. Arthur Whitney, Elwyn, Pa., was reelected secretary. The next annual meeting has been set tentatively for June 24-28, 1941, in Salt Lake City.——Dr. George M. Coates, Philadelphia, was chosen president of the American Otological Society at its annual meeting May 27. Dr. Isidore Friesner, New York, is secretary. The 1941 meeting will be May 26-28 in Atlantic City, N. J.——Dr. Harold Douglas Singer, Chicago, was designated president-elect of the American Psychiatric Association at its annual meeting, May 24, and Dr. George H. Stevenson, London, Ont., was installed as president. Dr. Arthur H. Ruggles, Providence, was reelected secretary. The next annual session will be in Richmond, Va.——Dr. Harold D. Corbusier, Plainfield, N. J., was reelected president of the Academy of Physical Medicine at its annual meeting in Richmond, Va. Drs. Gervase J. P. Barger, Washington, D. C., and Thomas F. Wheeldon, Richmond, were elected vice presidents. The 1941 meeting will be in New York.

LATIN AMERICA

Society News.—The first Brazilian Congress of Gynecology and Obstetrics will be held in Rio de Janeiro, September 8-15. Subjects to be discussed are recent advances in gynecologic endocrinology, diagnosis and treatment of cervical cancer, endocrinology in obstetrics and the social aspect of obstetric care. Dr. Arnaldo de Moraes, Rio de Janeiro, is president of the organizing committee.——Drs. Federico Gómez and Luis Berlanga Berumen, Mexico City, have been elected president and secretary, respectively, of the Mexican Society of Pediatrics for 1940-1941.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 15, 1940.

Internment of Alien Physicians and Nurses

The organized treachery employed in the attacks on small countries now known as "fifth column" activities has led to extensive precautions in Britian. These include the internment of all enemy aliens between the ages of 16 and 60 and restrictions on other aliens. This regulation has caused serious inconvenience to alien physicians and students. At the present time many are studying medicine at the Edinburgh school. Of these a large proportion are of German or Austrian nationality, mostly refugees from persecution. But it is not possible to be sure that some enemy emissaries are not among them, masquerading as refugees. For the safety of the country all aliens of enemy nationality have therefore to be interned. Some hold house appointments in the hospitals. Their internment will therefore cause inconvenience to the hospitals as well as to themselves. Aliens who are not of enemy nationality are not interned but their movements are restricted, as possibly they also may include dangerous elements. There are many American undergraduates at Edinburgh who are prohibited by the regulation from being outdoors after 8 p. m. At the medical school about fifty are working. Representations are being made on their behalf for some relaxation of the curfew. One of the grounds is that their freedom of movement at night is necessary for attendance at emergency work in the hospital. Twenty-nine sisters and nurses of the German Hospital, London, have been interned, following a visit of the police.

Second Removal of Children

The removal from London and other centers to places of greater safety from air raids of 1,270,000 persons in four days was described in THE JOURNAL May 25, page 2134. Of these nearly 1,000,000 were children. The evacuation was entirely voluntary but was strongly advised by the government and arranged by it in every detail. But many parents did not avail themselves of the scheme and about 800,000 children remained. As the expected air attacks did not materialize, many children were brought back to their homes. The approach of the war to our shores has caused the government to arrange a second evacuation of children. About 120,000 are now being removed from London, and the process is to be completed in a week. They are going west, the majority to Cornwall, Devon, Somerset and Wales, where they will be far from the areas considered dangerous. But it is estimated that there are still in London 300,000 children whose parents are unimpressed by the government appeals to register them for evacuation.

Wounded Brought From France to England

The emergency hospital scheme created for the care of civilian casualties and the great majority of military casualties is now receiving its first adequate test. During the past two weeks there have been received from France thousands of military casualties which have been distributed over fifty hospitals in Britain. In the House of Commons, the minister of health, Mr. Malcolm Macdonald, stated that the reception and care of the men from the battle line had worked smoothly and satisfactorily. French and other allied wounded who have been evacuated from Dunkirk have also arrived in England. In a broadcast an eminent surgeon, who, as usual in such cases, remains anonymous, assures the public that the wounded are having the best care that can be provided by a service which includes almost all the best brains in the medical profession.

Physical Therapy for War Injuries

Attention has been called in the press by surgeons and others to the need for adequate and early facilities for the physical-therapeutic treatment in hospitals of war injuries. On behalf of the Ministry of Health Sir George Chrystal, secretary, received a deputation of the Health and Housing Committee of the House of Commons, who came to emphasize this need. In reply Sir George Chrystal said that the ministry regarded it as essential that the scheme for the treatment of orthopedic and war strain injuries should provide for physical therapy not only in the early but in the recovery or convalescent stages. Patients with other types of injury would receive any necessary further treatment of this kind, either as outpatients at hospitals or from general practitioners. With regard to cases occurring in the armed forces, the ministry was planning their treatment with the War Office. At all the general hospitals in the Emergency Medical Service, massage and electrical treatment at the bedside were available. There were also nineteen special orthopedic centers at which massage, radiant heat, electrical treatment and remedial exercises would be available. At these centers there would be also departments for occupational treatment. The service provided five centers for war strain in addition to the effort syndrome center in London. Here remedial exercises and remedial occupations were being provided. These twenty-four centers were in different parts of the country. The intention was to transfer to them from the general hospitals all cases which required their special facilities. The ministry was now reviewing the hospitals with a view to ensuring that the necessary apparatus was available wherever necessary. The deputation expressed itself as satisfied that the ministry was bringing the standards in the emergency hospital scheme up to a high level.

Laurence O'Shaughnessy Killed in the War

One of the most brilliant of the younger surgeons, Mr. Laurence O'Shaughnessy, the thoracic surgeon, has been killed in Flanders while serving as a major in the Royal Army Medical Corps. He was only 39. He qualified F.R.C.S. at the age of 23. In 1924 he was appointed medical inspector in the Sudan, where he stayed for seven years. During this period he visited Sauerbruch's clinic and so became interested in thoracic surgery. He left the Sudan and spent six months with Sauerbruch and then obtained the Royal College of Surgeons research fellowship, which enabled him to do experimental work to the Downe research farm. In 1933 as Hunterian professor he lectured at the college on the surgery of the esophagus and two years later on the surgery of the root of the lung. He published a paper on traumatic shock which is considered classic. When the London county council, with the encouragement of Lord Dawson, formed a clinic at the Lambeth Hospital for the surgical treatment of cardiovascular disease, he was appointed consultant surgeon. He was also thoracic surgeon to the city of Birmingham tuberculosis scheme and various sanatoriums for tuberculosis. He did much work on the surgical treatment of tuberculosis and introduced the operation of thoracolysis. But it is for his work on the surgery of the heart, culminating in his operation of cardio-omentopexy, that he is best known. After much experimental work he introduced this operation to provide a collateral circulation in cases of cardiac ischemia with its resultant angina pectoris. In 1938 he was able to report twenty cases in which he had performed the operation. Those who survived the operation for one year, and in some cases for two years, at the time of the report continued to be active. The operation is of course a severe one for patients already debilitated by disease, and the general view is that its value still remains to be assessed. He published about thirty papers and wrote the section on the esophagus and diaphragm in Maingot's Post-Graduate Surgery. In 1937 he collaborated with Sauerbruch in a book on thoracic

surgery. He also collaborated with Kayne and Pagel in their book on pulmonary tuberculosis. It is a tragic irony that this man, who did so much to give credit to Germany for the surgery of the chest, should have died by German hands and from a wound in the chest.

SWITZERLAND

(From Our Regular Correspondent)

May 28, 1940.

Prevention of War Epidemics

Dr. Hermann Mooser, professor of hygiene, recently addressed the medical society of Zurich on the prophylactic measures employed at the present time against war epidemics. Mooser has had a wide experience in tropical regions and recently was in charge of a hygienic mission sent to China by the League of Nations. He pointed out that military forces fed under hygienic conditions may develop diseases of the digestive tract the infective agent of some of which had not yet been isolated. Intestinal inflammations of this kind do not last more than from twenty-four to forty-eight hours, are traceable to colds and have a benign evolution. In poisoning by meat caused by Salmonella enteritidis, Bacillus breslaviensis and Salmonella suipestifer, partly due to intoxication, partly to infection, animal paratyphosis is involved. New infections arise from this source. Infection by contact is infrequent. Carriers and excretors of bacilli are exceptional. Army physicians need to bear in mind that meats do not show signs of infection and that vegetables and pastry may also be at fault, if meat remnants, bouillon and so on are used in their preparation. Medical science is yet insufficiently informed about essential epidemiologic aspects of bacillary dysentery, in contrast with our knowledge regarding typhus infection, paratyphus infection and infection due to meat poisoning. At any rate the infectiousness of dysentery compared with that of other gastrointestinal diseases is exceedingly high. Mooser indicated that even in China it was more difficult to combat dysentery than cholera and typhus. The statistics of the World War showed that vaccinations against typhus and paratyphus greatly increased prophylaxis against epidemics. No doubt could any longer be entertained of the value of subcutaneous immunization against abdominal typhus and paratyphus; however, statistics on the efficacy of peroral immunization were still far from univocal. Prophylactic immunization against diphtheria has not been possible yet because of the variety of infectious agents and the intense local reactions. On the other hand, diseases of the respiratory tract are much more difficult to control. There is, however, an exceedingly great divergence between the number of infected and the number of manifestly ill persons. This is true not only for poliomyelitis but for cerebrospinal meningitis, designated by Mooser as a rare complication of infection of the nasopharyngeal passage due to meningococci. In poliomyelitis a fourteen day quarantine of the affected military force is the appropriate measure; in epidemic meningitis care must be added. Fatigue is known to create to a high degree a predisposition to the disease. Young recruits, unaccustomed to military strain and stress, are much more susceptible than soldiers in the regular service.

Anti Air Raid Hospital Planned

In consequence of the war, the erection of a large bomb proof hospital offering protection against air raids and capable of resisting the severest bombardments has been decided on in Basel, a city bordering on the German and French frontiers. Four entrances are planned to provide access and to meet the hazard of partial obstruction by débris. The equipment also is planned to meet the needs of battles on a large scale. Degassing of gassed persons is calculated to require, on the average, eight minutes. This will make possible the degassing of 3,000 persons daily. About 500 slightly wounded persons could be taken care of daily on a twenty-four hour working schedule and 100 operations of seriously wounded performed, with possible blood transfusions, in three planned operating rooms. The cost of construction is estimated at 800,000 Swiss francs (about $180,000).

Additional War Measures

All physically fit Swiss men have been called to the colors. However, they receive temporary furloughs and are subject to emergency recall. These regulations apply more or less also to the medical profession. Since the outbreak of the war, Swiss physicians have divided their time between their company and their private practice. Arrangements have been made for university students to continue their studies. Students required to take examinations in the spring were given furloughs. Other students receive furloughs good for two months. This enabled them to complete about half of a semester and was credited to them for a full semester's work. The Swiss federal government has also ordered special examination periods for medical students in preparation of the gaps caused by the mobilization of the medical profession. The practical half year required of all medical students has likewise been canceled for the duration of the war and two years following.

The section on war hygiene formerly belonging to the division of war welfare within the federal department of economics has been transferred to the federal health department. It is charged with hygienic problems that affect the welfare of the civilian population because of the military surveillance of the country's borders. It cooperates closely with the sanitary division of the army and with the sanitary service division (grenz-sanitätsdienst) operating on the borders. This last named division exercises health control jurisdiction over all persons entering Switzerland. Those suspected of an infectious disease are assigned for observation to certain hospitals within the border area. Similarly, persons attacked by a noninfectious disease are turned over by this federal agency to civilian hospitals.

The medical societies of Berne, Zurich and other cities largely concern themselves with problems arising from the war. Necessary sanitary measures are taken everywhere and pertinent discussions prepared. For example, the medical society of Geneva prepared a training course on war medicine and surgery. This course lasted a month and was conducted by specialists for Swiss army physicians, nearly all of whom are civilian practitioners. Prof. René Leriche, French surgeon of Strasbourg, was one of the lecturers.

Marriages

JAMES WILLIAM FOUCHE, Columbia, S. C., to Miss Lease Wyman of Greenwood in Aiken, June 8.

ROBERT HAL GINGLES, Oklahoma City, to Miss Helen Louise Wilson of Chickasha, Okla., May 30.

ALFRED STENGEL JR., Philadelphia, to Miss Anne Adele Hammett of Chestnut Hill, Pa., June 15.

MARCUS KELLOGG MOOKERJEE to Miss Marie Louise Borchardt, both of Milwaukee, May 4.

SAMUEL STUART DU PUY, Beckley, W. Va., to Miss Helen E. Baker of Morgantown, June 1.

MAX S. KRAUS, Rockaway Beach, N. Y., to Miss Caroline Gottlieb of New York, May 26.

JULIUS L. BOIARSKY, Charleston, W. Va., to Miss Hortense Marguerite Balacaier, April 14.

EUNICE LE BARON STOCKWELL to Mr. Walter Baker, both of Philadelphia, June 15.

WILLIAM HENRY LANE JR. to Miss Jane Zimmer, both of Indianapolis, May 25.

SAMUEL NIEDER, Gilman, Ill., to Miss Myrtle Levinson of Chicago, May 26.

Deaths

Calvin Brewster Coulter, Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1913; associate professor of pathology at the Long Island College of Medicine; associate in bacteriology at his alma mater, 1923-1924, associate professor of bacteriology from 1924 to 1934 and later associate professor of sanitary science; member of the American Society for Experimental Pathology; served during the World War; served at various times and in various capacities on the staffs of the Kings County Hospital, Long Island College Hospital, Nassau Hospital, Mineola, N. Y., Brooklyn Hospital and the Prospect Heights Hospital; aged 52; died, May 10, in the North Country Community Hospital, Glen Cove, N. Y., of pneumonia.

Bertram Lewis Bryant ✠ Bangor, Maine; Medical School of Maine, Portland, 1898; member of the House of Delegates of the American Medical Association from 1920 to 1923, from 1925 to 1928 and from 1930 to 1933; formerly secretary of the Maine Medical Association; past president of the Penobscot County Medical Association; consulting physician to the Waldo County Hospital, Belfast, and the Bangor State Hospital; medical director of the Bangor Sanatorium; aged 67; pathologist from 1899 to 1903, visiting physician from 1903 to 1934 and consulting physician since 1934 at the Eastern Maine General Hospital, where he died, May 10, of uremia.

William Albert Henke ✠ La Crosse, Wis.; Illinois Medical College, Chicago, 1906; University of Illinois College of Medicine, Chicago, 1913; past president of the Wisconsin Hospital Association and the La Crosse County Medical Society; for many years chairman of the county board of health; aged 59; medical director of the Grandview Hospital, where he died, May 8, of coronary sclerosis.

Donald St. Clair Campbell, La Plata, Md.; Dalhousie University Faculty of Medicine, Halifax, N. S., Canada, 1916; member of the Medical and Chirurgical Faculty of Maryland; deputy state health officer for Charles County; served during the World War; aged 46; died, May 15, in the Georgetown University Hospital, Washington, D. C., of hemorrhage due to esophageal varix.

John David Moore ✠ Bloomfield, N. J.; Yale University School of Medicine, New Haven, Conn., 1902; member of the American Academy of Ophthalmology and Otolaryngology; attending surgeon at the Newark Eye and Ear Infirmary, Mountainside Hospital, Montclair, and the Essex County Hospital for Contagious Diseases, Belleville; aged 64; died, May 12.

John Aloysius Sanders, Omaha; John A. Creighton Medical College, Omaha, 1911; for many years assistant in clinical obstetrics at his alma mater and instructor in anatomy in the dental school; on the staffs of the Nicholas Senn Hospital, St. Catherine's Hospital and St. Joseph Hospital; aged 55; died, May 23, in Sioux Falls, S. D., of carcinoma of the rectum.

Bernard W. Hays, Jackson, Mo.; University of Louisville (Ky.) Medical Department, 1894; University and Bellevue Hospital Medical College, New York, 1899; member and past president of the Missouri State Medical Association; on the staffs of St. Francis and Southeast Missouri hospitals, Cape Girardeau; aged 72; died, April 18, of coronary disease.

E. Weldon Young ✠ Seattle; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1889; fellow of the American College of Surgeons; on the staffs of the Maynard Hospital, Columbus Hospital, Swedish Hospital and the King County Hospital; aged 70; died, May 9, of hypertensive cardiovascular disease.

John Calvin Wright, Antigo, Wis.; Rush Medical College, Chicago, 1882; member of the State Medical Society of Wisconsin; formerly county physician, city physician and health officer; at one time secretary of the Langlade County Medical Society; aged 82; on the staff of the Langlade County Memorial Hospital, where he died, May 11.

Walter Otts Allen, Hendersonville, N. C.; Medical College of the State of South Carolina, Charleston, 1926; member of the Medical Society of the State of North Carolina; served during the World War; aged 42; died, May 13, in the Johns Hopkins Hospital, Baltimore, of petrositis and pneumococcic meningitis.

Len Lenton Culp ✠ Des Moines, Iowa; University and Bellevue Hospital Medical College, New York, 1889; Illinois Medical College, Chicago, 1900; formerly special physician at large for the Indian Service; member of the Indiana State Medical Association; died, May 10, of coronary thrombosis.

Logan B. Zintsmaster, Massillon, Ohio; Western Reserve University Medical Department, Cleveland, 1901; member of the Ohio State Medical Association; fellow of the American College of Surgeons; served during the World War; on the staff of the Massillon City Hospital; aged 63; died, May 10.

Hyman Israel Vener ✠ Los Angeles; University of Illinois College of Medicine, Chicago, 1925; assistant clinical professor of medicine, University of Southern California School of Medicine; member of the city health department; aged 40; died, May 23, in Cedars of Lebanon Hospital of uremia.

Clarence Sylvester Cook, Los Angeles; Chicago College of Medicine and Surgery, 1910; member of the California Medical Association; served during the World War; on the staffs of the Methodist Hospital, Queen of Angels Hospital and the French Hospital; aged 53; died, May 8.

Horace Clifford Stroup, Seward, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1925; served during the World War; on the staff of the Lee Homeopathic Hospital, Johnstown; member of the board of health of Seward; aged 43; died, May 5, of carcinoma of the rectum.

John Henry Weber, Akron, Ohio; Western Reserve University Medical Department, Cleveland, 1902; member of the Ohio State Medical Association; fellow of the American College of Surgeons; surgeon to the City Hospital; aged 62; died, May 13, of cerebral hemorrhage.

Morris Lee King, New Canaan, Conn.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1881; formerly medical director of the New York Life Insurance Company; aged 83; died, May 13, of cerebral hemorrhage and arteriosclerosis.

Harry Garfield Wright, De Kalb, Ill.; Hahnemann Medical College and Hospital, Chicago, 1907; at one time county coroner; formerly state senator; served during the World War; aged 58; died, April 17, in Holland, Pa., of heart disease, diabetes mellitus and kidney stones.

Max Emmert ✠ Omaha; Johns Hopkins University School of Medicine, Baltimore, 1909; fellow of the American College of Surgeons; surgeon to the Nebraska Methodist Episcopal Hospital; aged 56; died, May 16, in the Immanuel Hospital of coronary thrombosis.

Irving Darche ✠ Brooklyn; University and Bellevue Hospital Medical College, New York, 1928; assistant physician on the staff of the Beth-El Hospital; aged 38; died, May 17, in the Jewish Hospital of nasopharyngeal carcinoma with metastasis to the brain.

Albert W. Lewis Jr., Atlanta, Ga.; University of Tennessee College of Medicine, Memphis, 1932; member of the Medical Association of Georgia; assistant in pharmacology and in medicine at the Emory University School of Medicine; aged 29; died, May 13.

Hubert Sidney Smith, Thibodaux, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1898; member of the Louisiana State Medical Society; director of the Lafourche Parish Health Unit; aged 75; died, May 2, of coronary thrombosis.

Lincoln C. Chenoweth ✠ Joplin, Mo.; Missouri Medical College, St. Louis, 1886; an Affiliate Fellow of the American Medical Association; past president of the Jasper County Medical Society; aged 75; on the staff of St. John's Hospital, where he died, May 5.

William Baker Furman, Easley, S. C.; Medical College of the State of South Carolina, Charleston, 1908; member of the South Carolina Medical Association; county health officer; past president of the Pickens County Medical Society; aged 56; died, May 21.

Francis Edward Morgan, Santa Cruz, Calif.; University of California Medical Department, San Francisco, 1881; formerly county coroner, county physician, county and city health officer; aged 83; died, April 30, of chronic myocarditis and bronchiectasis.

James A. Christian, Dardanelle, Ark.; Kansas City College of Medicine and Surgery, Kansas City, Mo., 1921; formerly member of the state legislature; aged 44; died, May 2, in a hospital at Little Rock of coronary occlusion and ruptured appendix.

Morris Buist Garner, Madison, Tenn.; College of Physicians and Surgeons, Memphis, 1907; formerly a lawyer; member of the Tennessee State Medical Association; past president of the Middle Tennessee Medical Association; aged 61; died, May 11.

Patrick Francis Moylan, Scranton, Pa.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1890; member of the Medical Society of the State of Pennsylvania; aged 76; died, May 30, of carcinoma of the stomach.

Albert Milo Shattuck, Worcester, Mass.; Dartmouth Medical School, Hanover, N. H., 1895; member of the Massachusetts Medical Society; on the staffs of the Worcester City and the Memorial Hospital; aged 69; died, May 26, of arteriosclerosis.

Albert Joseph Vesely, Creve Coeur, Ill.; University of Illinois College of Medicine, Chicago, 1934; member of the Illinois State Medical Society; aged 32; was killed, May 18, when the automobile in which he was driving was struck by a train.

William Harland Emery, Coatesville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1896; aged 70; died, May 3, in the Chester County Hospital, West Chester, of myocardial degeneration and cirrhosis of the liver.

Thomas Melville Talbott, Falls Church, Va.; University of Maryland School of Medicine, Baltimore, 1870; member of the Medical Society of Virginia; aged 91; died, May 3, of fracture of the neck of the femur and bronchopneumonia.

William LeRoy Marks ⊕ Pittsburgh; University of Pennsylvania School of Medicine, Philadelphia, 1911; resident physician at Carnegie Institute of Technology; aged 55; died, May 23, in the Presbyterian Hospital of coronary thrombosis.

Milan Coburn, Coopersville, Mich.; Detroit College of Medicine, 1893; member of the Michigan State Medical Society; for many years health officer; aged 81; died, May 25, in Grand Rapids of coronary sclerosis and cardiac decompensation.

Nan Gilbert Seymour ⊕ New York; Cornell University Medical College, New York, 1902; medical director of the William Booth Memorial Hospital; aged 64; died, May 27, of lobar pneumonia, type III, and bilateral psoas abscess.

Howard Alfred Bayles, Port Chester, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1901; member of the Medical Society of the State of New York; aged 62; died, May 20, of metastatic carcinoma.

Wayne Neal Freemyer ⊕ Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1912; served during the World War; aged 56; died, May 30, in St. Vincent's Infirmary of nephrolithiasis with abscess and embolus.

Benjamin F. Shamblin, Lyerly, Ga.; Atlanta Medical College, 1888; member of the Medical Association of Georgia; aged 80; past president of the Chattooga County Medical Society; died, May 20, of carcinoma of the rectum.

Burnham Roswell Benner, Lowell, Mass.; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1875; member of the Massachusetts Medical Society; aged 93; died, May 29, of arteriosclerosis.

Robert M. McCreight, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1887; for many years police surgeon; aged 78; died, May 17, in St. Joseph's Hospital of hypertensive cardiovascular disease.

Cecil Claude Bowie, Carroll, Iowa; State University of Iowa College of Medicine, Iowa City, 1907; member of the Iowa State Medical Society; on the staff of St. Anthony Hospital; aged 59; died, May 24, of toxemia.

Fred Melvin Cole ⊕ Gardiner, Maine; College of Physicians and Surgeons, Boston, 1908; school physician; formerly health officer; on the staff of the Gardiner General Hospital; aged 61; died, May 5, of acute coronary thrombosis.

Adolph Steiner, Cleveland; University of Wooster Medical Department, Cleveland, 1891; for many years on the staff of the Mount Sinai Hospital; aged 72; died, May 16, of carcinoma of the sigmoid with metastasis to the liver.

Frank Ellis Estes, Compton, Calif.; Denver and Gross College of Medicine, 1904; veteran of the Spanish-American and World wars; for many years district health officer; aged 63; died, April 29, of coronary arteriosclerosis.

Benjamin H. Bainbridge, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1895; aged 71; died, May 29, in the Philadelphia General Hospital of bronchopneumonia and arteriosclerotic heart disease.

Edward Laurence Patterson, Fayetteville, Ark.; Atlanta (Ga.) School of Medicine, 1908; served during the World War; on the staff of the Veterans Administration Facility; aged 55; died, May 22 of coronary thrombosis.

Henry Edward Bittner, Hazleton, Pa.; Jefferson Medical College of Philadelphia, 1902; for many years member of the city board of education; aged 70; died, May 25, of arteriosclerosis and cerebral hemorrhage.

Theodore Francis Trimble, Corpus Christi, Texas; University of Rochester School of Medicine, 1932; member of the State Medical Association of Texas; aged 36; was killed, May 5, in an automobile accident.

Louis Howard Wilmot, Ansonia, Conn.; University of the City of New York Medical Department, 1891; city health officer; for many years on the staff of the Griffin Hospital, Derby; aged 70; died, April 23.

George A. Stanton, Belding, Mich.; St. Louis College of Physicians and Surgeons, 1893; past president of the Ionia County Medical Society; aged 82; died, April 21, in the Presbyterian Hospital, Los Angeles.

John Alexander Dales ⊕ Sioux City, Iowa; Rush Medical College, Chicago, 1890; fellow of the American College of Surgeons; on the staff of the Methodist Hospital; aged 79; died, May 13, of heart disease.

Hunter Robb Sunkle, Cleveland; University of Cincinnati College of Medicine, 1929; member of the Ohio State Medical Association; on the staff of the Lutheran Hospital; aged 36; died, May 15, of myocarditis.

Robert Arthur Haggard, Arcola, Miss.; Atlanta School of Medicine, 1912; member of the Mississippi State Medical Association; served during the World War; aged 56; died, May 15, of angina pectoris.

J. W. Wyman, Denmark, S. C.; University of Georgia Medical Department, Augusta, 1893; member of the South Carolina Medical Association; aged 67; died, May 1, in Columbia of cholelithiasis.

George W. Holt, Malabar, Fla.; University of Tennessee Medical Department, Nashville, 1901; veteran of the Spanish-American War; aged 61; died, May 11, of cerebral hemorrhage and chronic myocarditis.

Sanford W. Forbush, Beloit, Wis.; Northwestern University Medical School, Chicago, 1907; member of the State Medical Society of Wisconsin; aged 56; died, May 18, of coronary thrombosis.

William Sandusky ⊕ Seward, Neb.; John A. Creighton Medical College, Omaha, 1910; past president of the Seward County Medical Society; owner of the Seward Hospital; aged 59; died, April 28.

Malaku Emmanuel Bayen, New York; Howard University College of Medicine, Washington, D. C., 1935; aged 40; died, May 4, in the Rockland State Hospital, Orangeburg, N. Y., of lobar pneumonia.

Irving Masten Vanderhoff ⊕ Newark, N. J.; University and Bellevue Hospital Medical College, New York, 1905; on the staff of the Presbyterian Hospital; aged 58; died, May 2, of heart disease.

John McQuirk Leonard, Blairsville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1903; served during the World War; aged 61; died, May 21, of chronic pyelonephritis.

Emma Hammond Wheeler, New Bedford, Mass.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1893; aged 80; died, May 24, in Fairhaven of cerebral thrombosis.

I. Phillip Pollack, Hempstead, N. Y.; New York University College of Medicine, 1939; intern at the Meadowbrook Hospital; aged 24; died, April 21, of hemolytic streptococcus meningitis.

John Langland Lundby, Irwin, Iowa; Northwestern University Medical School, Chicago, 1910; member of the Iowa State Medical Society; aged 56; died, May 30, of coronary occlusion.

George Franklin Harding, Brookline, Mass.; Harvard Medical School, Boston, 1889; member of the Massachusetts Medical Society; aged 77; died in May of carcinoma of the prostate.

Francis Marion Frazier, Bryan, Ohio; Fort Wayne (Ind.) College of Medicine, 1891; also a lawyer; formerly judge of the court of common pleas in Williams County; aged 82; died, April 26.

George William Roland Bowie, Vanceboro, Maine; Jefferson Medical College of Philadelphia, 1934; member of the Maine Medical Association; aged 30; died in May of tuberculosis.

Jordan E. Ruhl, Kansas City, Mo.; Central Medical College of St. Joseph, Mo., 1903; Barnes Medical College, St. Louis, 1904; aged 71; died, May 30, of carcinoma of the prostate.

Ross B. Cobb, Philadelphia; University of Maryland School of Medicine, Baltimore, 1913; aged 69; died, May 19, in the Atlantic City (N. J.) Hospital of chronic myocarditis.

Robert Newton Pitts, Memphis, Tenn.; Atlanta Medical College, 1890; veteran of the Spanish-American War; aged 74; died, May 20, of coronary thrombosis and cardiorenal disease.

Howard Lewis Pintler ⊕ Peoria, Ill.; Hahnemann Medical College and Hospital, Chicago, 1901; aged 65; died, May 25, in St. Francis Hospital of diffuse fibrinopurulent peritonitis.

George Brookins, Caroga Lake, N. Y.; Albany (N. Y.) Medical College, 1894; aged 72; died, May 20, in the Montgomery Sanatorium, Amsterdam, of pulmonary tuberculosis.

Bernard Harrington Taylor ⊕ Marion, Ohio; St. Louis University School of Medicine, 1928; on the staff of the Marion City Hospital; aged 37; died, May 9, of angina pectoris.

Frank Smith Jennings, St. Petersburg, Fla.; University of the City of New York Medical Department, 1880; member of the Florida Medical Association; aged 81; died, May 9.

Wilton Daniel Garrett, West Winfield, N. Y.; University of the City of New York Medical Department, 1885; aged 83; died, April 8, of chronic nephritis and arteriosclerosis.

Linton Williams Struble, Davenport, Iowa; State University of Iowa College of Homeopathic Medicine, Iowa City, 1897; aged 73; died, May 12, of coronary thrombosis.

William Ernest Long ⊕ Pearland, Texas; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; aged 60; died, May 14.

Arthur Robert Higdon, Fancy Farm, Ky.; Hospital College of Medicine, Louisville, 1901; member of the Kentucky State Medical Association; aged 61; died, May 12.

George E. Willoughby, Gosport, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1905; aged 71; died, May 8, of coronary occlusion and arteriosclerosis.

Elmer John Austin ⊕ Fort Steilacoom, Wash.; University of Oregon Medical School, Portland, 1934; on the staff of the Western State Hospital; aged 47; died, April 29.

Ransom Joseph Parker ⊕ New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1893; aged 70; died, May 3.

William Barrett Acker, Hannibal, N. Y.; Bellevue Hospital Medical College, New York, 1894; health officer; aged 70; died, May 7, of coronary thrombosis.

Henry Vernon Logan, Miami Beach, Fla.; Medical College of Indiana, Indianapolis, 1897; served during the World War; aged 67; died, May 22, of myocarditis.

Quintus L. Shelton, Loneoak, Ky.; University of Tennessee Medical Department, Nashville, 1899; aged 73; died, May 23, of uremia due to hypertrophy of the prostate.

William Cook Martin, Kansas City, Mo.; Eclectic Medical University, Kansas City, 1912; aged 69; died, May 18, in Sabetha, Kan., of hemorrhagic nephritis.

Ernest Arnold Guyton, Eau Claire, Wis.; Saginaw (Mich.) Valley Medical College, 1900; aged 75; died, May 13, in the Luther Hospital of bronchopneumonia.

William Brehon Nash, Stanton, Tenn.; Vanderbilt University School of Medicine, Nashville, 1915; served during the World War; aged 48; died, April 30.

Auldy Theodore Rank, Van Wert, Ohio; Eclectic Medical Institute, Cincinnati, 1906; member of the Ohio State Medical Association; aged 61; died, April 25.

Nathaniel J. Ridley, Lexington, Ky.; Meharry Medical College, Nashville, Tenn., 1900; aged 73; died, May 23, of carcinoma of the abdominal viscera.

Arthur Denman Van Dyke ⊕ Scranton, Pa.; University of the City of New York Medical Department, 1883; aged 80; died, May 4, of coronary sclerosis.

Martha Rau Williams, Cincinnati; Laura Memorial Woman's Medical College, Cincinnati, 1897; aged 76; died, May 24, of chronic myocarditis.

Samuel B. Steele, Hot Springs National Park, Ark.; Louisville (Ky.) Medical College, 1894; aged 70; died, May 4, of chronic nephritis and uremia.

Arthur R. Wilson, Milwaukee; College of Physicians and Surgeons of Chicago, 1886; aged 83; died, May 8, of myocarditis and pernicious anemia.

Avery Leroy Myrick, Daytona Beach, Fla.; University of Alabama School of Medicine, 1910; aged 55; died, May 21, of hypertensive heart disease.

Benjamin F. McNeil, Des Moines, Iowa; University of Illinois College of Medicine, Chicago, 1902; aged 68; died, May 14, of arteriosclerosis.

Benjamin Hoff Searing, Newburgh, N. Y.; Cornell University Medical College, New York, 1903; aged 61; died, April 15, at St. Luke's Hospital.

Winfield Holmes Miller, Reno, Nevada; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1920; aged 43; died, May 16.

Whitfield Brooks Bean, Marianna, Ark.; Tulane University of Louisiana School of Medicine, New Orleans, 1894; aged 71; died, April 29.

Edgar J. Foote, Clarence, N. Y.; University of Buffalo School of Medicine, 1885; aged 80; died, May 1, in Buffalo of chronic myocarditis.

Thomas Jackson Hickman, Lenoir City, Tenn.; Tennessee Medical College, Knoxville, 1900; aged 80; died, May 8, in a hospital at Knoxville.

Charles Louis Weisberg, New York; University and Bellevue Hospital Medical College, New York, 1921; aged 42; died, April 30.

Lewis Nathaniel Foote, New York; New York University Medical College, New York, 1897; aged 67; died, May 6, of heart disease.

Thomas Davidson Macdonald, Central Valley, N. Y.; College of Physicians and Surgeons, Baltimore, 1904; aged 59; died in April.

Charles Sumner Laughlin, Vineland, N. J.; University of the City of New York Medical Department, 1878; aged 86; died in April.

Hugh N. Macdonald, Whycocomagh, N. S., Canada; Queen's University Faculty of Medicine, Kingston, Ont., 1882; died in May.

Theodore M. Wittkamp, Cincinnati; Cincinnati College of Medicine and Surgery, 1875; aged 86; died, May 21, of cerebral hemorrhage.

James William Nash ⊕ Buffalo; Niagara University Medical Department, Buffalo, 1894; aged 68; died, May 5, of coronary occlusion.

Clarence Ernest Pickett, Richland, Ga.; Atlanta Medical College, 1894; served during the World War; aged 69; died, April 26.

Eliphaz Cowan Forbes, Ardmore, Tenn.; University of Nashville (Tenn.) Medical Department, 1899; aged 73; died, April 13.

Lillian Garabrant Perry, Hingham, Mass.; New York Medical College and Hospital for Women, 1896; aged 70; died, April 11.

John Valanglingham Mott, Amelia, Ohio; American Eclectic Medical College, Cincinnati, 1885; aged 76; died, May 17.

Alfred Clinton Smith, Lanett, Ala.; Atlanta School of Medicine, 1912; served during the World War; aged 53; died, May 18.

Walter Fairfield Thomison, Dayton, Tenn.; Vanderbilt University School of Medicine, Nashville, 1892; aged 80; died, May 5.

Thomas Arlander Martin, Loraine, Texas; Vanderbilt University School of Medicine, Nashville, 1892; aged 73; died, May 4.

Walter Wilson Thompson, Niagara Falls, Ont., Canada; Trinity Medical College, Toronto, 1889; aged 72; died, April 25.

Thomas Stephen Hession, Peoria, Ill.; College of Physicians and Surgeons, Keokuk, Iowa, 1891; aged 70; died, May 14.

Thomas J. Haines, Three Rivers, Mich.; College of Physicians and Surgeons of Chicago, 1888; aged 86; died, May 22.

John Alexander Sandbach, Irvington, Ky.; Hospital College of Medicine, Louisville, 1904; aged 65; died, May 2.

Alfred Thompson, Vancouver, B. C., Canada; Halifax (N. S.) Medical College, 1898; aged 70; died, April 20.

John Douglas Berry, Willowdale, Ont., Canada; Trinity Medical College, Toronto, 1890; aged 77; died, May 1.

Arthur George Hubbard ⊕ Detroit; Maryland Medical College, Baltimore, 1900; aged 74; died, May 1.

A. Victory Seymour, Grosse Ile, Mich.; Detroit Homeopathic College, 1906; aged 55; died, May 28.

Bureau of Investigation

J. R. BREWSTER AND THE GOVERNMENT AGENCIES

His "Cures" Declared Fraudulent Again and Again by Post Office Department, While Food and Drug Administration also Objects (Unsuccessfully) and Federal Trade Commission Enters Complaint

Constant vigilance on the part of the Post Office Department is required to prevent individuals or companies whose fraudulent schemes have been debarred from the mails from continuing their businesses by operating under new names.

J. R. (Reese) Brewster and the Brewster Laboratories of Nashville, Tenn., conducted a mail order business in the sale of various nostrums which they falsely represented to cure tuberculosis, cancer, asthma and some other diseases. On Dec. 21, 1934, the Post Office issued a fraud order closing the mails to Brewster and his concern. Later, when it was discovered that Brewster was evading the order by continuing his fraudulent enterprise but using a new trade style, "New Deal Clinic," the original fraud order was extended to cover this name.

Again Brewster dodged! With Clyde Morris, said to be a relative, he was found to be running the same old fraud under still another name, "Dr. Reese Brewster." An inquiry addressed to that name brought the reply that the preparations supplied were the same as those sold for the previous fifteen years. The memorandum on the case reported that Morris admitted to the Post Office inspector that he was aware of the fact that fraud orders already had been issued against the scheme but that both he and Brewster intended to continue operating it unless stopped by conviction under the criminal statutes. Accordingly on Sept. 6, 1939, a supplemental fraud order was issued against the name Dr. Reese Brewster.

In an earlier case another government agency, the Food and Drug Administration, had seized interstate shipments of four nostrums sent out by J. R. Brewster when he was trading as Brewster Laboratories. Government chemists reported that the "Germ Destroyer" (for tuberculosis, cancer, asthma and some other things) contained a light petroleum oil, a saponifiable oil and turpentine; and that the three others were essentially similar in composition except that the "Throat Wash" (for tonsillitis and chronic throat trouble) also contained a trace of ferric chloride, the "Throat-Eaz" (for coughs, croup and "female trouble") included a trace of potassium iodide, and the "Liver Tonic" (for stomach disorders) contained no turpentine.

The government charged that the claims made for these products in the respective disorders named were fraudulent, but a jury in a district federal court brought in a verdict of not guilty.

In 1938 a third government agency, the Federal Trade Commission, also proceeded against what was apparently the same concern but at that time operating from Dallas, Texas. A release issued in September of that year reported that the Commission had entered a complaint against one Jefferson R. Brewster, who traded as Brewster Laboratories and Dr. Reece Brewster, charging misrepresentations in the sale of various nostrums. Among these were that "Brewster's G-D" is a protection against tuberculosis, a remedy for asthma, a relief of pain in any part of the body and, in combination with "Brewster's Tonic," a remedy for cancer; that "Brewster's T-Z" is a means of preventing or alleviating coughing spells and tubercular hemorrhages; that "Brewster's Sinine" is a treatment for sinus, mastoid, antrum, nose or ear trouble; that "Brewster's Pain Kill" is a treatment for rheumatism, neuritis and neuralgia and a cure for pneumonia and diphtheria; and that certain other Brewster preparations, not named, are treatments for kidney and stomach troubles, gallstones and goiter.

It was further charged that Brewster's products were not, as represented, prepared in laboratories nor had Brewster had medical training or laboratory experience and consequently was not qualified to practice medicine. Apparently this case has not yet been settled.

Just why the Food and Drug Administration was unable to prove Brewster's claims fraudulent in the eyes of the jurors whereas the Post Office was later able to issue a fraud order is not clear. At least it is reasonable to presume that the Federal Trade Commission was justified in entering a complaint charging misrepresentations in the sale of Brewster's nostrums.

Correspondence

DETERMINATION OF PROTHROMBIN

To the Editor:—From the literature and from our correspondence with many American investigators it seems that there have been several investigators who have had difficulty in understanding certain details in our method for the determination of prothrombin. As a number of methods have been suggested for this purpose, it might interest American investigators working on coagulation of human blood to hear about our experiences in this field.

It is now generally agreed that the methods usually employed so far in the clinic for determination of the coagulation time and bleeding time are not accurate enough for examination of avitaminosis K and that the prothrombin has to be determined, i. e. that primarily the plasma has to be obtained without any admixture of tissue extract, and then the prothrombin in this plasma is determined by examining its coagulation on addition of tissue extract. Methods that do not follow this principle are too inaccurate and unspecific to be serviceable for further investigation of the significance of vitamin K or for the daily work in the clinic.

In the preparation of prothrombin-free plasma it is essential, of course, to prevent spontaneous coagulation of the blood—for instance by addition of an anticoagulant. For this purpose Quick uses oxalate and subsequent recalcination simultaneous with the addition of tissue extract. We have found, however, that greater accuracy is obtained by using heparin. When heparin is used it is not necessary to add calcium. An amount of 0.03 mg. of pure heparin to 4 cc. of blood is sufficient to prevent spontaneous coagulation of the blood without preventing coagulation on addition of thrombokinase (tissue extract) when this substance is added in larger amounts than are normally present in the blood (platelets). Thus the influence of the number of platelets is eliminated. The greatest advantage from the use of heparin, however, is that one can choose the quantity of heparin such that the measured coagulation times will range, for example, from two to six minutes, while with most other methods one has to measure coagulation times of a magnitude of about ten seconds for normal blood, which may be done only with essentially greater inaccuracy. Here it is further to be mentioned that with our modification of the heparin method some very interesting information can be obtained about anomalies of the coagulation in a number of other disorders (e. g. hemophilia). This information about the qualitative and quantitative aspects of the anomalies of coagulation mentioned will contribute to elucidate the nature of these diseases—data that might not be obtainable with other methods for examination of the coagulation.

The coagulation anomaly in avitaminosis K is a diminution in the ability of the blood to coagulate on addition of tissue extract, i. e. that addition of a certain amount of tissue extract to a given amount of blood gives a longer coagulation time for the diseased blood than for the normal. The proportion between the two coagulation times is a direct expression for the coagulation anomaly. The lowered capacity for coagula-

tion with tissue extract may also be expressed in this way: that a greater amount of tissue extract—for instance, R times as much—has to be added to a certain amount of K avitaminotic plasma than to the same amount of normal plasma in order to make it coagulate within a certain length of time, say three minutes. Then the value R is a direct expression for the coagulation anomaly; and it is in this way that we have defined the coagulation anomaly in our studies. Many investigators have preferred, however, to reckon with the prothrombin content of the blood instead of with the "R value." It will be appropriate, therefore, to point out that the effective prothrombin content of the blood can be found also by means of the R value method. This is done by diluting normal plasma with plasma free from prothrombin (for example, plasma treated with aluminum hydroxide). On determination of the R value for a series of such dilutions, it is easy to find the prothrombin concentration giving the same R value as the plasma in question.

Now it turns out that the R value is approximately reversely proportional to the prothrombin content, so that an R value of X corresponds to 100 : X per cent of the normal prothrombin content. Thus analyses after the R value method are easily comparable to examinations giving the prothrombin content in percentage of normal. It is most rational, of course, to give the prothrombin content. So far we have preferred to express the coagulation anomaly by means of R values, partly because this means a direct expression for the coagulation anomaly but also because the coagulation of the blood is a far more complicated process, where the plasma exerts its influence on the coagulation time through many factors besides the prothrombin concentration. Here we have in mind the plasma component that is absent in hemophilia.

As to the value of determining the coagulation in clinical work after the principles outlined here, we think that it is essential always to keep in mind the great rapidity with which a fall in prothrombin may set in; this may occur also after an operation has been performed. It is to be emphasized that vitamin K therapy is to be instituted in every instance of obstructive jaundice even if there is no demonstrable decrease in prothrombin. So the significance of prothrombin determinations is merely that a decreased prothrombin is a warning against an operation, whereas normal values do not mean that the risk of fatal hemorrhage is excluded, unless a suitable vitamin K therapy is given.

Lately we have not published any data concerning the therapeutic aspects of the problem because Dr. Tage-Hansen, who has undertaken the clinical investigations, is going to publish a fairly comprehensive work on this subject. On account of the sudden great interest taken in the subject, he recently prepared a preliminary report of his studies, which was published in THE JOURNAL, Nov. 18, 1939, page 1875.

While it is true that ingestion of the vitamin together with bile salts acts more rapidly than intramuscular injections of emulsions, the main result of Tage-Hansen's work is that each of the three forms of administration has its particular advantages. Ingestion of vitamin K together with bile salts allows the use of rather crude vitamin K preparations but has the possible disadvantage of introducing extra bile salts into the organism. Intramuscular injection makes it possible to supply the organism with a store of vitamin K that is not absorbed so rapidly but the action of which lasts for weeks. Here oil may be used for the solutions. Intravenous injection of suitable emulsions has a very rapid effect, and it is possible by this method of introduction to use a smaller quantity than by ingestion.

HENRIK DAM.
JOHANNES GLAVIND.
Biochemical Institute, Copenhagen, Denmark.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SULFANILAMIDE THERAPY AND GRANULOCYTOPENIA

To the Editor:—**Perhaps a year ago, and prior and subsequent to that time articles were published in The Journal concerning the complications of sulfanilamide therapy, particularly in reference to granulocytopenia and hemolytic anemia. Is it not true that granulocytopenia is apt to appear later than the first week of therapy and anemia during the first week? If a white count during therapy is 5,000 or less, should sulfanilamide always be promptly stopped? If the count is found to be between 1,500 and 2,000 can one always expect granulocytopenia to develop—that is, after the patients have been on sulfanilamide and there are no other diseases present to account for the leukopenia? If sulfanilamide is stopped before granulocytopenia develops but after leukopenia is present, is there still danger of the former developing? How long before the danger is over? Is anemia likely to develop after therapy has been stopped?**

M.D., Iowa.

ANSWER.—In considering the changes which may occur in the blood of patients who are receiving sulfanilamide or its derivatives, it has been noted that acute hemolytic anemia generally occurs during the first five days of therapy, although one instance of this toxic manifestation has been reported on the twentieth day (Nelson, Edna L., and Scott-Young, Margery: *M. J. Australia* **1**:629 [April 2] 1938). Slowly developing hemolytic anemia may occur at any time during the course of treatment with these drugs. Acute leukopenia with granulocytopenia, while most frequently seen during the first ten days of treatment, may be seen at almost any time during a course. These acute leukopenias are rarely accompanied by angina and are characterized by the fact that the polymorphonuclear leukocytes do not as a rule disappear completely from the peripheral blood. In many clinics it is a rule that if the granulocytes drop below 50 per cent of the differential count in adults, or below 40 per cent in children, therapy with sulfanilamide or its derivatives should be stopped. It is also wise to check carefully the differential white blood cell count when the total white blood cell count drops below 5,000.

It does not always follow that with the development of low total white blood cell counts, i. e. from 1,500 to 2,000 cells, one should necessarily expect granulocytopenia accompanied by angina and the other severe symptoms of this blood dyscrasia. Almost all of the actual cases of granulocytopenia which have been reported as occurring in the course of therapy with sulfanilamide and its derivatives have appeared after the fourteenth day of treatment, with the seventeenth to twenty-fifth days of therapy being the most common time for the development of this toxic manifestation. If such a leukopenia is noted and sulfanilamide is stopped before the granulocytes disappear, in most instances the granulocytes continue to decrease and granulocytopenia with angina develops. When a leukopenia with granulocytopenia has been noted in the course of treatment with sulfanilamide or its derivatives and the drug has been stopped, if an increase in the polymorphonuclear leukocytes does not occur within thirty-six hours it is highly probable that a true granulocytopenia is developing. The period of granulocytopenia in these patients may last from one to seven days before a return of polymorphonuclear leukocytes is noted.

If an acutely developing anemia is not present at the time at which therapy with sulfanilamide or its derivatives has been discontinued, there is little chance of an acute hemolytic anemia developing. However, if it has been noted that an acute hemolytic anemia is developing and sulfanilamide is stopped because of this toxic manifestation, the anemia generally continues to progress for two or three days despite the fact that the drug has been stopped.

HUMAN TUBERCULOSIS IN CATTLE

To the Editor:—**Has there been any epidemiologic work done to show the amount of human tuberculosis in cattle and the hazard to cattle from farm employees with open tuberculosis?**

M.D., New York.

ANSWER.—Typing studies on the infecting organism in bovine tuberculosis show that it is regularly the bovine type of tubercle bacillus. Repeated experimentation has shown that the human type bacillus is of low infectivity for cattle. In almost all patients with open pulmonary tuberculosis in this country the infection is with the human type of tubercle bacillus. It seems

unlikely that a patient with this type of infection could infect cattle. T. G. Hull (Diseases Transmitted from Animals to Man, Springfield, Ill., C. C. Thomas, 1930) writes that "the human type of bacillus has never been found to infect cattle spontaneously." In other countries, however, where bovine tuberculosis is common, occasional cases of open pulmonary tuberculosis in man, due to infection with the bovine type of tubercle bacillus, occur. A. S. Griffith and W. T. Monro (The Relative Incidence of the Human and Bovine Types of Tubercle Bacilli in Human Tuberculosis in Scotland, *J. Path. & Bact.* **35**:271 [March] 1932) wrote that the infecting organism in open respiratory tuberculosis was bovine in type in 3.8 per cent of 548 cases in Scotland. It is possible that caretakers expectorating the bovine type tubercle bacilli may infect cattle.

Although it is generally agreed that infection with human type tubercle bacilli does not cause significant lesions in cattle, there is evidence that it may sensitize them to tuberculin. Apparently massive infection is required. A. B. Crawford (*J. Am. Vet. M. A.* **89**:562 [Nov.] 1936) found that about half of a group of bovine animals fed heavy doses of human type tubercle bacilli in sputum subsequently became tuberculin positive. The animals becoming allergic were not the ones receiving the heaviest dosage, but the dosage was large in all cases. Unless the feeding of bacilli was continued, sensitivity tended to disappear in a few months. At necropsy tuberculous lesions were not found. It has been reported from Finland (Stenius, R.: *Vet. Rec.* **50**:633, 1938) that in a certain herd attended by a tuberculous patient a large percentage of the cows reacted to tuberculin. After the death of the attendant, the percentage of reactors decreased rapidly without removal of cattle from the herd. Three years after the attendant's death, no cattle in the herd reacted to tuberculin. No lesions were found in these cattle, although an acid-fast bacillus considered to be a human type tubercle bacillus was isolated from the tissues of one reactor. Whether such cases as the latter are to be considered conclusive or not, in view of the proof that sensitivity may be induced by tubercle bacilli experimentally it appears possible that the sputum of a patient with open tuberculosis, carelessly discharged in the food of cattle, might make them sensitive to tuberculin, at least transitorilly.

TOXIC ADENOMA AND DIABETES

To the Editor:—**A white man aged 29, married, who is working in one of the local industrial plants, came to my office on Dec. 7, 1939, with the complaint of being 10 pounds under his usual weight. Except for nervousness, he had no other complaints. The blood pressure was 130 systolic, 80 diastolic, the pulse 92 per minute, the heart regular in rate, rhythm and force, the weight 128 pounds (58 Kg.) the thyroid enlarged, and there was a palpable adenoma of the right lobe and isthmus. The heart was synchronous with the pulse rate and there were no adventitious sounds. There was slight tenderness over the cecum and lower portion of the descending colon. Urinalysis showed 1 per cent of sugar present. December 14 the basal metabolism, determined at the local hospital, was + 38. The fasting blood sugar was 185 mg. Because of the high basal rate I prescribed an organic iodine preparation. On Jan. 11, 1940, the urine was sugar free but the fasting blood sugar was 175 mg. On February 19 the basal metabolism was + 38 per cent. He weighed 131 pounds (59 Kg.) the blood pressure was 120/80 and the pulse 68. There was no evidence of thyrotoxic symptoms. The urine was negative for sugar. On February 27 a sugar tolerance test revealed: fasting specimen, 188 mg.; one-half hour after taking dextrose, 208 mg.; one hour after taking dextrose, 204 mg.; two hours after taking dextrose, 179 mg.; three hours after taking dextrose, 185 mg.; four hours after taking dextrose, 188 mg. Could this be hyperglycemia due to an increased activity of the thyroid gland or could it be possible that both diabetes mellitus and an overactive thyroid exist without manifestations of thyrotoxicosis? If there is any literature that you can refer to on this matter, I shall appreciate it.**

M.D., Pennsylvania.

ANSWER.—Glycosuria and hyperglycemia may occur in the presence of hyperthyroidism. In some instances this may reflect the influence of the increased metabolism. In others, particularly following the giving of dextrose, it may represent the tendency recently pointed out by Althausen, Lockhart and Soley (A New Diagnostic Test [Galactose] for Thyroid Disease, *Am. J. M. Sc.* **199**:342 [March] 1940), who have demonstrated that in hyperthyroidism there is an increased rate of absorption of dextrose from the gastrointestinal tract. Blood sugar values above normal are obtained when dextrose is given orally and not when given intravenously.

Despite these considerations, in the case under discussion a diagnosis of diabetes mellitus is justified because the fasting blood sugars were 175 and 188 mg. per hundred cubic centimeters and even after the administration of dextrose the four hour value was still equal to that before the dextrose was administered.

The two basal metabolic rates, each plus 38 per cent, in addition to a palpable adenoma, suggest thyrotoxicosis, and it seems as though removal of the adenoma should lessen the severity of the diabetes somewhat but not eradicate it.

LATENT INFECTIONS

To the Editor:—**A white man aged 69 fell acutely ill with fever, chills, nausea, vomiting and headache. He was first seen about two hours later. At first a relevant past history was not obtained. Examination revealed temperature 101.6, pulse 92, respirations 24, blood pressure 140/75. The head and neck were normal, the lungs clear to percussion and auscultation, the heart one fingerbreadth enlarged to the left. A slight systolic murmur over the apex in the sixth left interspace, and perpetual arrhythmia were noted. The abdomen was normal. There was a small area of erythema over the right lower tibia. The white blood count was 17,400 with 75 per cent polymorphonuclears. The urine was normal except for the sediment, which was loaded with pus cells and after being stained showed the presence predominantly of gram-positive cocci resembling staphylococci. Urinary symptoms were not complained of by the patient. On rectal examination the prostate was not enlarged, was not tender and showed no evidence of tumor or abscess. Within twenty-four hours there developed a cellulitis of the right lower leg with the classic signs of pain, swelling and redness. Lymphangitis proximal to the knee was not present but the vessels of the extremity between the ankle and knee joints were palpable and appeared indurated. The tibia was tender to pressure in its entire length. At this time the following additional history was obtained, after a small, innocent looking, slightly atrophic scar had been found over the midportion of the right tibia: Two months prior to the onset of the acute illness the patient injured his right leg by striking it against the sharp edge of his working table in the factory where he is employed. This resulted in a superficial abrasion requiring only self treatment by cleansing the wound with witch hazel. Uneventful healing occurred within a few days, leaving the scar described. In the light of these occurrences a provisional diagnosis of cellulitis and (metastatic?) urinary tract infection was made. Under sulfanilamide therapy and symptomatic measures the temperature fell to normal, the urine cleared and the cellulitis slowly resolved. X-ray examination two weeks after the onset of the acute illness showed no bone involvement, ruling out osteomyelitis. Except for a slight, noninflammatory, residual edema the patient completely recovered. A final diagnosis conforming to the provisional one was made. Blood cultures had not been taken because under the sulfanilamide therapy which was instituted at once no further chill or excessive rise in temperature occurred. The questions arise whether the minor injury to the right leg, having occurred two months previous to the development of cellulitis of the same extremity, can be considered a causative factor, in which case the patient would be entitled to workmen's compensation benefits. The patient's illness resembled septicemia, but (a) would it be possible for an infection to remain dormant for two months before causing the clinical picture described? (b) Can the original injury be regarded as contributing to if not solely causing the patient's illness (locus minoris resistentiae)? (c) If both questions are to be answered in the negative, what other etiology for cellulitis plus (metastatic) urinary tract infection would have to be considered in this case? (d) Are any similar cases on record? If so, please advise where I can find references.**

M.D., New York.

ANSWER.—The case as described is complex and may be regarded from several points of view: 1. The abrasion may indeed have been a port of entry for an infection which later caused cellulitis and metastatic infection of the urinary tract. Latent infections of various kinds are known to exist for months or years, but in the case in question it seems unlikely that the trauma to the leg is important. The lesion was apparently superficial and healed promptly.

2. Infections anywhere in the urinary tract are not uncommon in a man 69 years old, particularly if obstruction is present, but no evidence of obstruction appears in the data given. When urinary tract infection is present, thrombophlebitis with cellulitis of the leg may complicate the picture as a secondary process, either as a metastatic localization during bacteremia or as the result of the abnormal rapidity of blood clotting with thrombus formation as an after-effect of infection.

3. If the vessels of the leg were palpable and indurated as mentioned, it is possible that latent thrombophlebitis may have been the source of a metastatic infection somewhere in the urinary tract, but not necessarily related to local trauma two months previously. If more careful bacteriologic studies had been made and the same kind of bacteria had been present in the two lesions, a relationship might be assumed with more assurance. For the same reason one cannot give credit to sulfanilamide for a cure in this case.

4. It is possible that the transient infection in the urinary tract and the cellulitis of the leg may both have been metastatic localizations of a blood borne infection arising elsewhere in the body.

To answer the questions raised, (*a*) it would be possible for infection to lie dormant, but improbable in this case according to the circumstances mentioned. (*b*) It is unlikely that the minor injury to the leg played any part in the condition described. (*c*) Already answered. (*d*) No cases of this sort have been found in the literature. Both conditions are so common as to make special reports unnecessary.

FREQUENCY OF SPINA BIFIDA

To the Editor:—I should like to have some information on the frequency of occurrence of spina bifida. I have examined several textbooks without finding any figures. M.D., Illinois.

ANSWER.—Grinker's Neurology states that spina bifida occurs in 0.1 per cent of children; defects of closure of the various arches occur in the following proportion: cervical region 9.5 per cent, thoracic region 4.5 per cent, lumbar region 34 per cent, lumbosacral region 24 per cent and sacral region 23 per cent.

Woltman has stated that spina bifida is responsible for a sixth of the monstrosities encountered (Woltman, H. W.: Spina Bifida: A Review of 187 Cases, Including Three Associated Cases of Myelodysplasia Without Demonstrable Bony Defect, *Minnesota Med.* **4**:244 [April] 1921).

Spina bifida occulta exists unrecognized in many instances throughout life and may or may not cause symptoms. Spina bifida occurs most frequently in the lumbar and sacral regions. No doubt the incidence of spina bifida varies considerably in the type of practice encountered.

DERMATITIS FROM CHEMICALS IN WATER

To the Editor:—Several miners, who have been working in a wet place underground, have developed severe dermatitis. The analysis of the water is as follows:

Total solids, nonvolatile	23.546 Gm. per liter
Total solids, as sulfates	29.406 Gm. per liter
Bicarbonate, HCO_3	0.0610 Gm. per liter
Bromide, Br	0.3572 Gm. per liter
Chloride, Cl	14.937 Gm. per liter
Sulfate, SO_4	0.2229 Gm. per liter
Silica, SiO_2	Trace
Iron and alumina Fe_2O_3 and Al_2O_3	0.0280 Gm. per liter
Calcium, Ca	6.2324 Gm. per liter
Magnesium, Mg	0.6177 Gm. per liter
Sodium, Na	1.5632 Gm. per liter
These are probably combined as:	
Sodium chloride, NaCl	4.099 Gm. per liter
Magnesium chloride, $MgCl_2$	2.419 Gm. per liter
Calcium chloride, $CaCl_2$	16.761 Gm. per liter
Calcium bromide, $CaBr_2$	0.447 Gm. per liter
Calcium bicarbonate, $Ca(HCO_3)_2$	0.081 Gm. per liter
Calcium sulfate, $CaSO_4$	0.353 Gm. per liter
Ferric sulfate, $Fe_2(SO_4)_3$	0.070 Gm. per liter

What would cause the burns and what local treatment would be advisable? M.D., Michigan.

ANSWER.—The dermatitis may be caused by one or all three of the following chemicals: magnesium chloride, calcium chloride and calcium bromide. Magnesium chloride partially decomposes in the presence of water into hydrochloric acid and magnesium oxychloride. Calcium chloride is a dehydrator, and calcium bromide decomposes under the action of carbon dioxide into hydrobromic acid and this on oxidation into free bromine.

Patch testing with the concentration of these chemicals found in the water may disclose which of them are the irritants. If it does not, a patch test with all three combined may show that it is their combined action on the skin which is causing the dermatitis.

Local treatment consists in removing the patient from his work and applying soothing applications such as boric acid solution or calamine lotion in the exudative stage, and boric acid ointment or Lassar's paste when the lesions are dry. Prevention consists in wearing waterproof coveralls or clothing and daily change to fresh work clothes.

SYMPTOMS AFTER REMOVAL OF NARCOTIC ADDICTION

To the Editor:—A woman aged 45 was a year ago completely removed from morphine, to which she had been addicted for nearly ten years. Late in her addiction she had taken as much as 25 grains (1.6 Gm.) daily by hypodermic injection. During the year since the withdrawal of the drug she has complained of severe pain in both shoulder joints, extreme nervousness, anorexia, insomnia and weakness. Careful study does not uncover any lesions to account for her symptoms. X-ray examination does not show any bone changes in the shoulder joints although motion apparently is painful. What are the usual effects on a patient who has for years taken large daily doses of morphine but who is finally cured of the addiction? Does the drug bring about any permanent pathologic changes when used for long periods? M.D., Iowa.

ANSWER.—The habitual use of any narcotic produces a moral, mental and often physical deterioration, the latter chiefly due to a lack of proper nutrition, bad sanitation and irregular habits. Morphinism is not so much a disease in and of itself as chronic alcoholism, which produces a demonstrable pathologic change. Persons who have once had an addiction are prone to believe that any mental or physical stress that they have needs quick narcotic relief and are often unwilling or think they are unable to carry on without the quick relief and comfort that narcotics give. Asthenia, insomnia and nervousness with pain or distress in different locations are common complaints of addicts after denarcotization. The fact that this patient used as much as 25 grains of morphine a day proves that she belongs to the type of individual with but little will power. There is no real physical need of an addict taking more than 8 or 10 grains (0.6 Gm.) of morphine a day. The excess does not give any real relief but often produces toxic symptoms.

RHEUMATIC FEVER AND PHYSICAL ACTIVITY

To the Editor:—About six months ago I took care of a case of acute rheumatic fever in a girl 10 years of age. The onset simulated infantile paralysis, there being apparent inability to use the lower limbs, some neck rigidity and high fever. The spinal fluid, however, was normal. The sedimentation rate at the onset was 35 mm. in one hour. After four weeks in bed the rate became normal. She was kept in bed another two weeks. No murmur was heard at any time. There was reduplication of the second sound in the third interspace, left, during the febrile stage. What is the modern tendency with regard to exercise and athletics in a child who seems to have an intact heart and is in good health otherwise? Is it wise to permit hand ball, basketball, tennis, swimming and are all restrictions in this respect removed? M.D., Wisconsin.

ANSWER.—The answer to this question is given without reference to the diagnosis of rheumatic fever in this particular case, for an insufficient amount of information is given for one to be certain of this diagnosis. The onset and short course of the disease are rarely encountered in children with rheumatic fever.

As a general rule, children with rheumatic fever have clinical or laboratory evidence of active disease for a few months at least. Rest is generally accepted as being wise as long as any evidence of infection persists. After active rheumatic fever subsides, a gradual increase in physical activity is the usual procedure. In a child without heart disease and no clinical or laboratory evidence of active rheumatic fever there is little evidence that any type of exercise is harmful to the patient. A recurrence of rheumatic fever is the possibility to be feared, and this is often associated with respiratory infection. Exercise apparently plays little or no part in such recurrences of the disease.

GAS COOKING RANGE FOR DRY STERILIZATION

To the Editor:—In the home in obstetric cases I use a small sterile pack which contains four towels, one small sheet, a cap, a gown and a mask. It is necessary to return these to my hospital many miles away for resterilization after they have been used. We have in our home a modern gas cooking range with an oven which has a dial heat control mechanism which starts in as low as 250 F. Could I use this dry heat for resterilization of these obstetric packs? What temperature should be used? For what length of time should it be used and would it destroy the fabric of the materials in the pack? Of course the materials are all cotton. All articles of the pack are simply covered with a muslin binder pinned well. Bruce I. Ryder, M.D., Henry, Ill.

ANSWER.—There is no better method of sterilization than by dry heat for those objects which are not injured by it, such as clean glassware, clean bandages or towels, and even petrolatum. The temperature required is about 320 F. (160 C.) for a period of two hours. The packs should not be larger than necessary and should not be closely crowded in the oven. It may be that white cotton goods will become slightly brown, especially after repeated sterilization, but it has not been found to injure the fabric except in appearance. The muslin binder should be thick enough to avoid contamination of the contents of the pack during handling after sterilization. The gas cooking range described should be satisfactory for this purpose.

BIO LAB SYPHILIS TEST

To the Editor:—What can you tell me regarding the Bio Lab Syphilis Test, using one drop of blood? It seems as though several doctors over the country have bought the outfits and I am wondering if it is reliable and dependable. The makers are Bio Chemical Laboratories, Inc., Dayton, Ohio. E. H. Brubaker, M.D., Flora, Ind.

ANSWER.—The Bio Lab Syphilis Test is published as a modification of the Ide test (Ide, Sobei, and Ide, Tamao: Ide Test—the New Color Test for Syphilis, *J. Lab. & Clin. Med.* **21**:1190 [Aug.] 1936) without stating what the modification is. The test is claimed to be "accurately diagnostic," but the literature on the Ide test is not unanimous on its value. The test is not supposed to require "specialized training," but tests for syphilis are based on complex interactions between colloids and they do require specialized training. The Ide or Bio Lab tests are not included among those which have been evaluated during the past five years by the American Evaluation Committee on tests for syphilis, which is functioning under the auspices of the U. S. Public Health Service, and no literature is available on the accuracy of the Bio Lab test.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, July 6, page 78.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II, Sept. 11-13. Part III, June or July, to be given in medical centers having five or more candidates desiring to take the examination. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Written.* Various centers, Feb. 20. Final date for filing application is December 21. *Oral.* Cleveland, preceding A. M. A. convention. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: December 1940. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* October 21. Applications must be on file not later than September 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Chicago, Oct. 18-19. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Cleveland, Oct. 5. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and written.* New Orleans, January 1941. Final date for filing application is November 15. Sec., Dr. Fremont A. Chandler, 6 N. Michigan Ave., Chicago.

AMERICAN BOARD OF PEDIATRICS: Memphis, Tenn., Nov. 17, preceding the annual meeting of the American Academy of Pediatrics. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* New York, December 18-19. Final date for filing application is October 8. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Boston, Sept. 26-29. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Part I. Various centers, October 21. Final date for filing application is September 15. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Oral and Written.* Chicago, February 1941. Applications must be on file not later than Oct. 15. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

New York Endorsement Report

Mr. Herbert J. Hamilton, chief, Bureau of Professional Examinations, reports 105 physicians licensed by endorsement from January 15 through March 30. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists		(1934), (1937)	N. B. M. Ex.
College of Physicians and Surgeons of San Francisco		(1909)	California
Yale University School of Medicine		(1936), (1937)	N. B. M. Ex.
George Washington University School of Medicine		(1936)	Maryland, (1937) New Jersey
Georgetown University School of Medicine		(1932)	Dist. Colum., (1933) Pennsylvania, (1936), (1938, 3) N. B. M. Ex., (1938) New Jersey
Howard University College of Medicine		(1935)	Tennessee, (1939) North Carolina
Emory University School of Medicine		(1938)	N. B. M. Ex.
University of Georgia School of Medicine		(1934)	Georgia
Northwestern University Medical School		(1937)	California, (1939) N. B. M. Ex.
Rush Medical College		(1934)	Minnesota
University of Illinois College of Medicine		(1924)	Michigan, (1938) Indiana
State University of Iowa College of Medicine		(1933)	Iowa
University of Louisville School of Medicine		(1936)	N. B. M. Ex.
Johns Hopkins Univ. School of Med.		(1919), (1934), (1939)	Maryland
University of Maryland School of Medicine and College of Physicians and Surgeons		(1935)	New Jersey. (1937), (1939, 2) Maryland
Boston University School of Medicine		(1938)	N. B. M. Ex.
Harvard Medical School		(1932)	Penna., (1933) N. B. M. Ex., (1936) North Carolina
Tufts College Medical School		(1914)	Georgia, (1938) N. B. M. Ex.
University of Michigan Medical School		(1925), (1929, 2)	Michigan
Wayne University College of Medicine		(1939)	Tennessee
St. Louis Univ. School of Med.		(1938)	N.B.M.Ex., (1939, 4) Tennessee
University of Nebraska College of Medicine		(1920)	Nebraska
Columbia Univ. College of Physicians and Surgeons		(1937)	N. B. M. Ex.
Cornell University Medical College		(1938)	N. B. M. Ex.
Long Island College of Medicine		(1938, 4)	N. B. M. Ex.
New York Medical College and Flower Hospital		(1936, 2), (1937, 4), (1938, 3)	N. B. M. Ex.
New York Medical College, Flower and Fifth Avenue Hospitals		(1939)	Maryland
University of Buffalo School of Medicine		(1938)	N. B. M. Ex.
University of Rochester School of Medicine		(1934)	N. B. M. Ex., (1936) New Jersey
Duke University School of Medicine		(1937)	N. B. M. Ex.
Eclectic Medical College, Cincinnati		(1938), (1939, 5)	Ohio
Ohio State University College of Medicine		(1937)	Ohio
University of Cincinnati College of Medicine		(1939)*	Ohio
University of Oklahoma School of Medicine		(1933)	Oklahoma
University of Oregon Medical School		(1937)	Maryland
Jefferson Medical College of Philadelphia		(1928), (1932)	Penna., (1932) Connecticut
Medical College of the State of South Carolina		(1920)	Minnesota, (1933, 2) South Carolina
Baylor University College of Medicine		(1938)	Texas
University of Texas School of Medicine		(1936)	Texas
Marquette University School of Medicine		(1939)	N. B. M. Ex.
University of Manitoba Faculty of Medicine		(1929)	Saskatchewan
Laval University Faculty of Medicine		(1931)	Connecticut
McGill University Faculty of Medicine		(1934)	N. B. M. Ex.
Medizinische Fakultät der Universität Wien		(1935)	Maryland
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin		(1920)	Germany, (1924) N. B. M. Ex.
Kaiser-Wilhelms-Universität Medizinische Fakultät, Strassburg		(1905)	Ohio
Ludwig-Maximilians-Universität Medizinische Fakultät, München		(1937)	New Jersey
Universität Heidelberg Medizinische Fakultät		(1914)	New Jersey, (1930) Ohio
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest		(1924)	New Jersey
Regia Università degli Studi di Firenze. Facoltà di Medicina e Chirurgia		(1928)	New Jersey
Regià Universita degli Studi di Modena. Facoltà di Medicina e Chirugia		(1927)	New Jersey
American University of Beirut School of Medicine		(1934)	N. B. M. Ex.
Licentiate of the Royal College of Physicians and of the Royal College of Surgeons of Edinburgh and of the Royal Faculty of Physicians and Surgeons of Glasgow		(1936)	Tennessee
Université de Lausanne Faculté de Médecine		(1935), (1937)	New Jersey, (1936) Ohio

* This applicant received the M.B. degree and will receive the M.D. degree on completion of internship.

Tennessee March Report

Dr. H. W. Qualls, secretary, Tennessee State Board of Medical Examiners, reports the written examination held at Memphis, March 20-21, 1940. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Twenty-five candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1939)	85.3
New York University College of Medicine		(1938)	88.2
University of Tennessee College of Medicine		(1940)	83.6, 84.1, 84.3, 85.3, 85.4, 86.1, 86.2, 86.2, 87, 87, 87, 88, 88.1, 88.2, 88.3, 89.3, 89.5, 89.5, 90.1, 90.9, 90.9, 91.3, 91.8

Six physicians were licensed by endorsement from February 2 through April 27. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois		(1898)	Illinois
University of Louisville School of Medicine		(1935)	Kentucky
Johns Hopkins University School of Medicine		(1936)	Maryland
University of Michigan Medical School		(1937)	Maryland
Ohio State University College of Medicine		(1935)	Ohio
University of Tennessee College of Medicine		(1937)	N. B. M. Ex.

Oregon January Report

Miss May Casey, assistant secretary, Oregon State Board of Medical Examiners, reports the written examination held at Portland, Jan. 9-11, 1940. The examination covered eleven subjects and included seventy-two questions. An average of 75 per cent was required to pass. Two candidates were examined, both of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
University of Oregon Medical School		(1935)	89
University of Wisconsin Medical School		(1937)	86

Eight physicians were licensed by reciprocity and three physicians were licensed by endorsement from January 10 through April 10. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical Evangelists		(1939)	California
State University of Iowa College of Medicine		(1938)	Iowa
University of Minnesota Medical School		(1929)	Minnesota
University of Nebraska College of Medicine		(1935)	Nebraska
University of Oregon Medical School		(1933), (1934)	Washington
University of Manitoba Faculty of Medicine		(1925)	Arizona
University of Toronto Faculty of Medicine		(1934)	Minnesota

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Washington University School of Medicine		(1934), (1935)	N. B. M. Ex.
Duke University School of Medicine		(1938)	N. B. M. Ex.

Book Notices

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association for 1939 with the Comments That Have Appeared in The Journal. Cloth. Price, $1. Pp. 205, with 5 illustrations. Chicago: American Medical Association, 1940.

Only seven of the thirty-five reports listed in this annual collected report are of the familiar "Not Acceptable" or condemnatory type. Two reports announce omission of products from N. N. R., one being off the market. The remainder, far superior in bulk as well as in number, are concerned with educational and constructive considerations. This trend has been noticeable in recent years; it reflects the great predominance of the constructive over what may be called the destructive side of the Council's work of promoting rational therapeutics.

The educational reports touch three fields on which lie the front lines of present day therapeutics progress—chemotherapeutics, endocrines and vitamins. Two reports on sulfapyridine deal with the status and Council acceptance of commercial brands. The report on Neoprontosil recognizes that term as the Winthrop Chemical Company's proprietary name for 4-sulfonamide benzene-2-azo-1-hydroxy-7-acetylamino naphthalene-3:6-*di*sodium sulfonate, and azosulfamide as the nonproprietary name for the same substance. The articles on Dilantin Sodium, Sobisminol Mass and Sobisminol Solution are status reports which accompanied the descriptions of accepted brands, a type of article increasingly used by the Council. Dilantin sodium is the new drug used in the treatment of epilepsy and has been accepted by the Council with carefully stated limitations for its use; sobisminol mass and sobisminol solution are new soluble bismuth preparations for use in the treatment of syphilis; they are noteworthy in that sobisminol mass has been shown to be effective when used orally. The reports on racéphedrine and nikethamide deal with nomenclature; these terms are recognized as nonproprietary names for racemic ephedrine (the sulfate and hydrochloride are also recognized) and pyridine-β-carboxylic acid diethylamide respectively; the latter was introduced into medicine under the proprietary name Coramine-Ciba and was the subject of a preliminary report by the Council in 1929 (THE JOURNAL, June 1, 1929, p. 1837).

The status report on questions concerning vitamins compiled by the Cooperative Committee on Vitamins of the Councils on Pharmacy and Chemistry and on Foods is becoming an almost annual event, awaited for the revisions of the "Allowable Claims" found acceptable for the various vitamins. This year's revisions are not extensive but the report is noteworthy for the reemphasis of the Council's stand on the subject of vitamins and vitamin mixtures. Alas, the Councils' is but one clear, authoritative voice of rationality in today's whirlwind of polyvitamin and polyvitamin-mineral absurdities foisted on the gullible public by astute and sophisticated advertising technic. The preliminary and supplementary reports by Snell and by Snell and Butt on the new principle for active hemorrhagic diathesis known as "vitamin K" are timely and noteworthy.

The leadership of the Council in matters of endocrine therapeutics and nomenclature is well sustained by such reports as Chorionic Gonadotropin, Assay Standards for Chorionic Gonadotropin, Stilbestrol and the Present Status of Testosterone Propionate: Three Brands, Perandren, Oreton and Neo-Hombreol Not Acceptable for N. N. R. No brand of any of these has been accepted and these reports are excellent justification of the Council's intelligent and well informed conservatism in this as in other matters.

Three "special" reports are worthy of mention. One is the warning report on the danger of intra-urethral injection of solutions of local anesthetics, a reaffirmative strengthening of previous Council pronouncements. One is the Council statement Manganese in the Treatment of Dermatologic Disorders, which is buttressed by the conclusive and well documented paper of Dr. Maurice Sullivan, considered and sponsored by the Council. The third is the Study of the Promiscuous Use of the Barbiturates, Their Use in Suicides, a paper by Dr. W. E. Hambourger based on a review of medical literature and study of vital statistics. This study was authorized by the Board of Trustees of the A. M. A. and will be followed by other papers dealing with other aspects of the problem.

The present annual volume of Council reports is somewhat larger than usual and somewhat above the average issue in interest.

Good Health and Bad Medicine: A Family Medical Guide. By Harold Aaron, M.D., Medical Consultant to Consumers Union of United States, Inc. Cloth. Price, $3. Pp. 328. New York: Robert M. McBride & Company, 1940.

This book, designed as a family medical guide, contains much interesting information. It is composed for the most part of what should be, by this time, well known suggestions for the maintenance of health. In some respects it goes further than the ordinary health guide, especially as it attempts to inform the reader of objectionable items which he might otherwise purchase for self medication for treatment of his own condition. Other items are recommended with carefully guarded statements as to the limitations of their use. In some cases the references for this evaluation of products include the various Councils, Bureaus and laboratories of the American Medical Association, but, needless to say, for the most part they are based on the reports of Consumers Union itself.

The book opens with a section on first aid and a description of a family medicine cabinet. This is followed by clearcut discussions of the various symptoms and disorders which are all too frequently cared for by self medication. The author is careful to warn repeatedly that certain conditions require the immediate attention of a physician and that others require his services if they are not amenable to the simplest remedies. In connection with dentifrices, the reader is referred to the American Dental Association, and for hearing aids, air filters and acceptable sun lamps for home use to the American Medical Association's Council on Physical Therapy. The vitamin preparations included are those which appeared in New and Nonofficial Remedies for 1939, and the author concurs in the Council on Pharmacy and Chemistry's decisions with regard to the "shot-gun" vitamin preparations. Warnings against the use of stimulants and drugs such as acetanilid and the bromides are well detailed. On the subject of diabetes the author lists all the remedies which have been declared to be fake or totally worthless by either the Council on Pharmacy and Chemistry or the Bureau of Investigation of the American Medical Association. The author concludes by stating that, if consumers learn from this book that medical advice appearing in advertisements should be taken with the proverbial grain of salt, the author will consider his work a success. It is doubtful whether he realizes that he has failed to include definite statements suggesting where additional information may be obtained concerning "patent medicines" and the advertising claims made for them.

There are some statements in the book which are open to question. For example, "The new Food and Drug law does not require that the presence of quinine be stated on the label" and "The only drug remedy that has been found to be of real value in the treatment of a cold is a combination of codeine and papaverine, or codeine alone." With some exceptions, however, the author's statements are in accordance with scientific fact.

La selva peruana: Sus pobladores y su colonización en seguridad sanitaria. Por el Dr. Carlos Enrique Paz Soldán, director, y Dr. Maxime Kuczynski-Godard, jefe de laboratorios del Instituto de medicina social de la Universidad de San Marcos, Lima. Paper. Pp. 68, with 100 illustrations. Lima: Ediciones de "La Reforma Médica," 1939.

This is a general discussion of the Indians of the Peruvian selva and of the possibilities for colonizing the selva. The latter is made up of the mysterious tropical lands near the Amazon River, which are rich in natural resources and apparently not good for the health of Peruvians other than the autochthonous Indians. The first chapter is by Professor Kuczynski-Godard, head technician of the Laboratories of the Instituto de Medicina Social of the University of San Marcos of Lima and also head of a scientific expedition to the selva which was organized by the institute as a preliminary survey in relation to colonization of the selva. The chapter is an ecologic study and a report of observations carried on during a long stay of the expedition in the selva, on the actual living

conditions of the people in relation to the cosmologic, geologic and social environment and also in relation to regional pathology. The second chapter is written by Dr. Carlos Enrique Paz Soldán, head of the Instituto de Medicina Social of the University of Lima and also organizer of the scientific expedition to the selva. The illustrations were taken during the expedition to the colony of the Perené River. They show beautiful scenes of the selva mountains and river, different racial types of Indians, housing of colonists and Indians and Indians suffering from regional diseases, most frequently malaria and ancylostomiasis. The whole collection of illustrations appears to be an ethnographic atlas of the Peruvian oriental selva.

Applied Anatomy: Functional and Topographical. By Robert H. Miller, M.D., Associate Professor of Anatomy in the University of Tennessee College of Medicine, Memphis. Cloth. Price, $6.50. Pp. 484, with 71 illustrations, including 16 colored plates. Philadelphia: Lea & Febiger, 1938.

Dr. Miller was a surgeon. He is now a professor of anatomy; this book indicates that he has long been a biologist. Evolution, both anatomic and physiologic, comes in for nearly as much consideration as does clinical anatomy. The book deals with those facts of anatomy which are of most biologic significance or of most direct clinical application. It is briefer than are most textbooks on the subject because it makes no attempt to be encyclopedic, but it is well arranged and covers the important parts of the field. The views expressed are logical and documented by constant references to recent literature. Medical students will find it interesting, instructive and a valuable introduction of clinical work. It will be of great service to them in directing their attention to those relatively few among the inumerable anatomic facts which are most valuable, significant and applicable. Physicians will be interested in the presentation of the biologic as contrasted with the clinical view of many of the discussions.

The Surgery of Pain. By René Leriche, M.D., LL.D., F.R.C.S., Professor of Clinical Surgery, University of Strasbourg, Strasbourg. Translated and edited by Archibald Young, B.Sc., M.B., C.M., Regius Professor of Surgery, University of Glasgow, Glasgow. Cloth. Price, $6.50. Pp. 512, with 18 illustrations. Baltimore: William Wood & Company, 1939.

The author is a person whose name has been associated for many years with the subject and who has written many articles on the theoretical, practice and experimental aspects of this problem. He is a worldwide authority on the subject at hand. From the nature of the book, which is really a series of lectures based on a theory of pain with an attempt at scientific investigation and compilation of facts, it is apparent that one must read the book in order to follow logically the author's concepts. The reader will be conscious of the enthusiasm of the author and will be easily and quickly won over. The practical application of the theory is not quite as convincing because of the elusive nature of pain. Leriche attacks the problem of pain not merely as a symptom but as a disease entity. The first two chapters cover the problem of pain in the light of surgical investigation and the physiologic condition of the pain—malady—general considerations regarding the surgery of pain. His work included ramisections which in the past decade have been supplanted by ganglionectomies because of surgical convenience and also splanchnic resections. He discusses surgery of the sympathetics and of the endocrines, especially adrenals and parathyroids. His diagnostic and therapeutic methods of local infiltrations with procaine hydrochloride and of direct infiltrations of the sympathetic trunks has been remarkably useful. The chapters on clinical entities include trifacial neuralgia, post-traumatic progressive spreading neuralgias, nerve injuries, causalgia and painful amputation stumps. Several chapters are devoted to vasoconstriction and such entities as Raynaud's disease and scleroderma. The subjects of arteritis and angina pectoris are well worth reading because of the insight into the cause of pain and the methods of obtaining relief. There are a chapter on cutaneous cicatrices and several chapters on visceral pain. The book closes with the pain of inoperable tumors and its treatment and a chapter entitled "What is Physical Pain?" In the translator's preface there is much praise for the author's work and great respect for his theories and practice in the alleviation of pain through the attack on the sympathetics and in the diagnostic value of the abolition of pain by regional infiltration with procaine. The book can be recommended highly for its attempt to solve the problem of pain, and the author will undoubtedly contribute more and more toward the alleviation of pain with the progress of time.

Fractures. By Paul B. Magnuson, M.D., F.A.C.S., Associate Professor of Surgery, Northwestern University Medical School, Chicago. Third edition. Cloth. Price, $5. Pp. 511, with 317 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1939.

The author adheres to his original purpose in writing this book, which was to present the subject from a broad point of view. He calls attention to the fact that the approach to the problems in the treatment of fractures has gone through a state of evolution, and he incorporates these trends in the present edition. The author presents those methods which he has found from experience to be worthy of trial. He has made a considerable addition to the discussion of first aid in the treatment of compound fractures, emphasizing the necessity for standardization of metal plates. The section on pathologic changes occurring in fracture lesions has been revised in accordance with the views of the American College of Surgeons. The operative treatment of fractures of the head of the humerus and the treatment of both bone fractures of the forearm by use of Kirchner's method are discussed. The section on fractures of the neck of the femur, a subject on which the author has written much good material, is also amplified. The whole work has been rewritten and reillustrated. The numerous beautiful line drawings by Shepard are especially clear and instructive.

Histological Technique for Intracranial Tumours. By Dorothy S. Russell, M.D., Member of Scientific Staff, Medical Research Council, Attached to Bernhard Baron Institute of Pathology, the London Hospital. Cloth. Price, $2.50. Pp. 71, with illustrations. New York & London: Oxford University Press, 1939.

This purely technical book should be of great value to all histologic technicians. It contains most of the recognized technics for the gross and microscopic preparation of all types of neurologic specimens with such personal modifications as Dr. Russell has deemed valuable in her extensive experience. She is to be especially commended for her appreciation of the limitations of classifications of such specimens by pure histologic staining methods. She is also wise in adding methods of rapid sectioning of tissues for immediate study during operations. Fortunately she considers the immediate practical value of her technical procedures rather than pure academic research, although many of the technics might well be used for that purpose. The book contains six photographic plates which serve as excellent examples of beautiful histologic and photographic technic.

Orthodigita: Procedure and Technique. An Introductory Text for Students and Practitioners of Podiatry. By Harry S. Eisenberg, Pod.G. Paper. Price, $1.50. Pp. 166, with 158 illustrations. Brooklyn, N. Y.: The Author, 1939.

The author defines the title of his book as a study of the development of the toes. He seeks to determine factors which determine the growth of toes to the end that normal, functional and anatomic relationship between the toes and the foot may be realized. He considers the subject a biologic problem with mechanical aspects. The aims and benefits of orthodigita are said to be the correction, restoration of function, treatment and prevention of foot deformities, relief from pain, and the elimination of deformities. Most of the diagrams are crude and many fail to instruct. The book is of no value whatever to the practicing physician.

Foot Orthopaedics. By Otto N. Schuster, Litt.B., Pod.G., Adjunct Professor Podiatric Orthopaedics, The First Institute of Podiatry, New York. Edited by Maurice J. Lewi, M.D., and Herman Scheimberg, M.Cp. Second edition. Cloth. Price, $7. Pp. 525, with illustrations. Albany, N. Y.: J. B. Lyon Company, 1939.

The author has made numerous additions to the first edition of his book. Several chapters have been rewritten, new illustrations added and some old ones deleted. One of the added chapters deals with the application of plaster of paris in relation to foot appliances. Many roentgenograms have been included in this edition. Many of the subjects are discussed briefly, which is necessary in order to keep the book within the confines of a handy volume. It is not clear why surgical procedures such as the Whitman astragalectomy are given in a book for chiropodists.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Liability of Employer for Medical and Hospital Treatment in Excess of Statutory Period.—In the course of her employment, Feb. 21, 1936, the plaintiff was struck on the head by a broken belt. The industrial commission of North Carolina approved an agreement for compensation entered into between her and her employer. While she was under treatment for her industrial injury a "serious mental disorder" developed and she was institutionalized in two different private sanatoriums. In February 1938, the employer petitioned the industrial commission for a release from liability for the expense of further medical and hospital treatment, contending that he had furnished treatment for the time required by the Workmen's Compensation Act of North Carolina and that unless further treatment would "tend to lessen the period of disability" he was not liable for further expenses. After a hearing, during which the testimony of three physicians was heard, the industrial commission denied the petition and found that the plaintiff was suffering from an incurable mental condition, dementia praecox, and that it was necessary to provide her "some kind of care at all times." The commission ordered the plaintiff transferred to the State Hospital at Morgantown, N. C., which transfer was made July 1, 1938, and further ordered the employer and his insurer, the defendants, to pay the cost of such hospitalization. The defendants then appealed to the superior court, Gaston County, which remanded the cause to the commission for a finding as to whether or not additional hospitalization and treatment would tend to lessen the period of disability. The commission without hearing further evidence made a specific finding that "additional hospitalization and treatment would tend to lessen the period of disability," and the defendants appealed again to the superior court, Gaston County. From a judgment of that court sustaining the commission's finding, the defendants appealed to the Supreme Court of North Carolina.

The questions to be determined, said the Supreme Court, are: 1. Is there sufficient competent evidence to support the commission's finding that additional hospitalization and treatment would tend to lessen the period of plaintiff's disability? 2. If not, when the industrial commission finds that a claimant is permanently and totally disabled as a result of an accidental injury arising out of and in the course of employment may the commission in its discretion award medical, surgical, hospital and other treatment for an indefinite period of time? Section 25 of the workmen's compensation act of North Carolina requires an employer to provide a workman injured in the course of his employment with necessary medical and hospital care "for a period not exceeding ten weeks from date of injury to effect a cure or give relief, and for such additional time as in the judgment of the commission will tend to lessen the period of disability." It is plain from this language that medical, surgical, hospital and other treatment must be provided by the employer for a period of ten weeks if such treatment is necessary to effect a cure or to give relief. Treatment may not be required for an additional time unless it "will tend to lessen the period of disability." Whether such additional treatment will tend to lessen the period of disability is a question of fact to be ascertained by the industrial commission on competent evidence. The court, however, did not believe that the commission was warranted in the instant case in making the finding that it did as to the effect of additional hospital treatment to be rendered to the plaintiff. All the physicians who testified before the commission agreed that the plaintiff's condition is incurable, that her psychosis is beyond human control and can be influenced only in minor features by treatment of any kind and that nothing remains to be done but to provide custodial care. There was no evidence whatever before the commission that further treatment would tend to lessen the period of the plaintiff's disability. On the contrary, the commission stated in the course of its first finding that the plaintiff had "sustained an injury by accident arising out of and in the course of her employment, resulting in permanent total disability." That finding terminated the liability of the employer for further treatment.

Another provision of section 25 of the workmen's compensation act provides that "in case of a controversy arising between the employer and employee relative to continuance of medical, surgical, hospital, or other treatment, the Industrial Commission may order such further treatment as may in the discretion of the commission be necessary." In the judgment of the court this provision must be read in connection with the rest of that section. When so considered, the exercise of discretion by the commission as to the necessity for treatment beyond the ten weeks' period can come into play only on a proper finding by it that additional treatment "will tend to lessen the period of disability." As already stated, such a finding in the instant case was not supported by the evidence.

The court accordingly, in effect, relieved the employer and his insurer from liability for further treatment and custodial care.—*Millwood v. Firestone Cotton Mills (N. C.), 2 S. E. (2d) 560.*

Workmen's Compensation Acts: Death from Unintentional Poisoning While Under Treatment for Industrial Injury.—A workman in the course of his employment sustained an industrial injury which necessitated the amputation of a portion of a toe six months later, May 26, 1936. His attending physician directed him to bathe the affected foot in a solution of mercury bichloride at stated times and gave him tablets of mercury bichloride with which to prepare the solution. Later the physician prescribed "sedative tablets" to be taken if the patient became uncomfortable from pain. The physician discharged the patient, June 16, "although the wound was still healing." On June 20, while intending to take a "sedative tablet" to relieve his pain, the workman by mistake swallowed a mercury bichloride tablet and died as a result thereof. His widow's claim for compensation under the New York workmen's compensation act for his death was denied by the State Industrial Board and she appealed to the supreme court, appellate division, third department, New York.

From the evidence adduced, said the court, it was apparent not only that the pain which the workman suffered following the amputation but also the taking of the sedative were the result of the employment. The painful injury and the attempt to minister thereto flowed directly from the employment. The catenation from the original industrial accident to the death about six months later was continuous. Had the physician by mistake administered the mercury bichloride tablet in place of a sedative the right to an award would not be open to question. *Parchefsky v. Kroll Bros., Inc., 267 N. Y. 410, 196 N. E. 308.* The court could see no distinction in the fact that the workman made the same mistake while attempting to relieve his pain in the manner and with a medicine prescribed by the physician. The court held that the death under the circumstances was compensable as an accidental injury arising from employment, and so it remanded the case to the industrial board for further proceedings in harmony with its decision. Subsequently the industrial board awarded compensation to the widow, which award was affirmed by the supreme court.—*Brown v. New York State Training School for Girls (N. Y.), 11 N. Y. S. (2d) 849; 19 N. Y. S. (2d) 901.*

Society Proceedings

COMING MEETINGS

American Congress of Physical Therapy, Cleveland, Sept. 2-6. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.
National Medical Association, Houston, Tex., Aug. 12-16. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.
Utah State Medical Association, Ogden, Aug. 29-31. Dr. D. G. Edmunds, 610 McIntyre Bldg., Salt Lake City, Secretary.
Virginia, Medical Society of, White Sulphur Springs, W. Va., July 29-31. Miss Agnes V. Edwards, 1200 East Clay St., Richmond, Secretary.
Washington State Medical Association, Tacoma, Aug. 26-28. Dr. V. W. Spickard, 1305 Fourth Ave., Seattle, Secretary.
West Virginia State Medical Association, White Sulphur Springs, July 29-31. Mr. Joe W. Savage, Public Library Bldg., Charleston, Executive Secretary.
Wyoming State Medical Society, Sheridan, Aug. 11-13. Dr. M. C. Keith, State Department of Health, Cheyenne, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

59:931-1166 (May) 1940

Congenital Cranial Osteoporosis: Its Etiology and Significance: Study of 800 Newborn Infants. O. Reiss and Elena Boder, Los Angeles. —p. 931.

Study of 240 Breast-Fed and Artificially Fed Infants in the St. Louis Area: II. Incidence of Rashes and Gastrointestinal Disturbances in Breast-Fed Infants and in Infants Fed on Fresh Milk Formulas and on Acidified (Lactic Acid) and Nonacidified Evaporated Milk Formulas. Edith C. Robinson, St. Louis.—p. 1002.

Factors Influencing Appearance of Centers of Ossification During Early Childhood: II. Comparative Study of Degree of Epiphysial Ossification in Infancy Under Varying Conditions of Diet and Health. C. C. Francis, Cleveland.—p. 1006.

*Enuresis: Study of Causes, Types and Therapeutic Results. L. Stockwell and C. K. Smith, Kansas City, Mo.—p. 1013.

*Tuberculosis: Follow-Up Study of Children at Lymanhurst Health Center. C. A. Stewart, Minneapolis.—p. 1034.

Interchangeability of Zinc Crystalline Insulin and Amorphous Insulin. R. L. Jackson, J. D. Boyd and Thelma Smith, Iowa City.—p. 1050.

Probable Mechanism of "Physiologic" Hypoprothrombinemia of the Newborn. L. M. Tocantins, Philadelphia.—p. 1054.

Gonorrheal Vaginitis in Children: Review of Literature. R. A. Benson and I. Weinstock, New York.—p. 1083.

Enuresis.—From an analysis of 100 representative children observed in the enuresis clinic Stockwell and Smith discuss the psychosomatic significance, the types of enuresis, the known facts about bladder function, the causative factors and the results of treatment. Enuresis in their experience is of three types: organic, 13 per cent; neuromyogenic, 37 per cent, and psychogenic, 50 per cent. Diagnosis of the type of enuresis before treatment is instituted is extremely important. A simple cystometric examination was a distinct aid in the analysis of function. The average age of the patients (sixty-three boys and thirty-seven girls) was 9 years. In fifty-nine who later had enuresis normal control had once developed—at the age of 16½ months in boys and 17½ in girls. Forty-one had nocturnal enuresis only, forty-seven nocturnal enuresis plus diurnal frequency but not incontinence; ten diurnal as well as nocturnal enuresis and two diurnal but not nocturnal enuresis. The therapeutic methods in addition to correction of physical defects and simple training are: (1) for the spastic bladder, atropine therapy plus aqueous distention, (2) for the atonic bladder, stimulation of the neck of the bladder and in severe cases mecholyl (acetylbetamethylcholine) and acetylcholine, (3) for the strongly expulsive bladder of small capacity, simple regular aqueous distention and (4) for nocturnal enuresis plus poor sphincter action, physiologic dosage of morphine at bedtime. Treatment was directed toward establishing a conditioned reflex by developing in the child a strong conscious effort to control the distended bladder, an effort which establishes neural pathways and cerebral interpretation of vesical function. This treatment worked best on essentially normal bladders. Patients with definite psychogenic enuresis responded well to simple psychotherapy, encouragement, education and adjustment of personal and social problems. Results indicated that 64 per cent of the patients were cured and 21 per cent improved (14 per cent of these had recurrences occasionally); 15 per cent were classed as unsatisfactory for various reasons.

Tuberculosis in Children.—Stewart analyzed the records of 10,003 children who entered the Lymanhurst Health Center between May 1921 and July 1932. The ages ranged from 3 months to 20 years and averaged 9 years. Initial reactions to tuberculin were negative for 7,107 and positive for 2,896. Initial roentgenograms of the chest were made of 84.3 per cent of the uninfected and of 95.5 per cent of the infected children. The lungs of 92.9 per cent of those with negative reactions and 57 per cent of the tuberculin-sensitive group were interpreted as normal. The incidence of roentgenographically demonstrable lesions considered nontuberculous tended in general to increase gradually in successive age groups. Relatively benign pneumonic infiltrations of pulmonary tuberculosis were found in 166 members of the infected group. The incidence of such lesions reached a maximum at about the third year of life and then diminished. The general tendency of these lesions was first to persist and later to resolve slowly. Calcified and fibrosed deposits were revealed by 2.8 per cent of the initial roentgenograms of the children with negative reactions, increasing slightly with advancing age. Calcified and fibrosed deposits were disclosed by 30.6 per cent of the initial roentgenograms of the infected children, increasing rapidly until the age of 8.5 years, after which it showed no consistent change. The initial roentgen study of 2,767 of the tuberculous children disclosed forty-nine with chronic pulmonary tuberculosis of the adult type. This form of the disease made its first appearance at the seventh year of life and tended to increase in relative frequency in each successive age group. Follow-up data derived from repeated roentgen studies, tuberculin tests or verbal inquiry were obtained for 80.9 per cent of the children with negative reactions and for 85.2 per cent of the infected group. The uninfected group were traced for an average of 6.1 years and the infected group for 6.9 years. Chronic pulmonary tuberculosis was acquired by sixteen of the 5,747 traced children whose initial tuberculin reactions were negative. Of the 2,467 traced children with initial positive reactions, 2,418 presented no evidence of chronic pulmonary tuberculosis at the time of the first examination. During the course of the follow-up study such disease was acquired by fifty-eight. During the follow-up the incidence of roentgenographically normal lungs decreased from 53.9 to 36.9 per cent in the infected group and the incidence of primary pneumonic tuberculous infiltrations decreased from 7.9 to 0.7 per cent. This change resulted from spontaneous resolution. The incidence of calcified and fibrosed deposits changed from an initial 31.6 per cent to a final 53.1 per cent. This change resulted from the appearance of these lesions in many of the infected children whose initial roentgenograms revealed no pathologic conditions. The incidence of chronic pulmonary tuberculosis increased from 2.7 to 6 per cent. During the course of the follow-up study chronic pulmonary and miliary disease, tuberculous meningitis and osteo-articular tuberculosis were acquired by nineteen members of the originally uninfected group and by ninety-eight members of the infected group.

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Scalenus Anticus Syndrome With and Without Cervical Rib.—Donald and Morton studied twenty-one cases of the cervical rib and scalenus anticus syndrome. Of the sixteen patients that have already received operative treatment, thirteen were without cervical ribs, two showed supernumerary ribs and one presented an abnormal first rib. This indicates that the scalenus anticus syndrome occurs much more frequently than do cervical ribs. Two of the remaining five cases, in which operation has been temporarily postponed, showed x-ray evidence of a cervical rib. The ages of the twenty-one patients ranged from 15 to 54 years, with an average of 37 years. The majority occurred in the fourth (nine) and fifth (five) decades. Direct trauma preceding the onset of symptoms could be demonstrated in only one of the twenty-one cases. In two others the trauma was attributed to faulty position while under anesthesia, followed immediately by the development of symptoms typical of the syndrome. Excessive occupational strain was a significant factor in eight cases. The preponderance of cases in the fourth and fifth decades may possibly be attributed to regressive muscular changes that occur at this time and result in drooping of the shoulders. The characteristic increase of pain at night may be accounted for by pressure from behind as the shoulders are brought forward against the scalenus anticus muscle while in the prone position. The symptoms of cervical rib and scalenus anticus syndrome are similar and in view of the fact that the scalenus anticus muscle is the primary factor in the production of neurocirculatory compression, whether a cervical or an abnormal first rib is present, it would seem appropriate to group the two conditions under the term "scalenus anticus syndrome," designating whether a cervical rib or an abnormal first rib is present. The surgical indications (scalenotomy) are the same and results are usually excellent. Fourteen patients have had complete relief from symptoms. Scalenotomy is not indicated in all cases, as many are mild and will respond to conservative therapy. The symptoms in the milder cases are not progressive but subject to remissions and exacerbations. Because of the frequent gradual onset and bizarre picture a positive diagnosis is often difficult. A neurologic examination is indicated in all cases. Conditions causing difficulty in the differential diagnosis are infectious neuritis, arthritis of the shoulder joint, cervical arthritis, subacromial bursitis and neurosis.

Cervicobrachial Syndrome.—Aynesworth believes that the Naffziger classification, neuritis of the brachial trunks, of the scalenus syndrome is too limited and that the vascular and nerve trunk symptoms should be expressed by a more inclusive term. The term "cervicobrachial syndrome" does not define the disease but it does give a comprehensive and an anatomic concept which is accurate and inclusive. The author has observed twenty cases in which the diagnosis was confirmed by operation or subsequent history. Sixteen of these patients have come under observation since the role of the scalenus anterior muscle has been understood. Of ten patients operated on, all but one were relieved of symptoms. The exception had only partial relief. X-ray examinations on patients not operated on confirmed the presence of cervical ribs when present and the neurologic and vascular examinations elicited the same observations as on patients operated on. All gave a history of traumatism. The symptoms under the heading cervicobrachial syndrome may be classified into neurologic symptoms, vascular symptoms or a combination of the two. These classifications arise from and are an expression of the major pathologic changes of the disease. The causes are similar but the pathologic processes are different. Compression of nerve tissues produces numbness, pain, paralysis and loss of function; compression of vascular structures results in moderate pain, edema, swelling, obstruction of the blood flow ending in clotting in the vessels and, if serious enough, death of the tissues supplied by these vessels. The location of the pathologic changes is confined to a small area, but one which is full of nerves and blood vessels, surrounded by muscles and osseous structures which have undergone great and vital changes in the course of evolution and embryology. Many of the diseases in this small region are the result of developmental defects. The theories of the etiology of the cervicobrachial syndrome are: (1) compression of the nerve trunks, (2) injury to the nerve trunks, (3) injuries to the sympathetic and the vasomotor nerves, (4) traumatism of the scalenus anterior muscle, (5) embryologic defects, (6) postural or functional defect, (7) narrowing of the upper thoracic cap as a result of adjacent infections or anatomic defects, (8) acute infections producing myositis and (9) intermittent traumatism to the subclavian artery.

Penetrating Wounds of Abdomen.—Storck reports forty-six cases of penetrating wounds of the abdomen, thirty-five of which were gunshot and eleven stab wounds. The symptoms associated with penetrating wounds of the abdomen are frequently indefinite. Pain is often slight or absent. Wounds which occur by way of the gluteal, sacral or perineal regions are particularly likely to be overlooked because early symptoms are frequently absent. The recognition of associated injuries, particularly those of the chest, is important in the management. Exploratory celiotomy should be performed when uncertainty concerning penetration of the abdomen exists. A short interval between the time of injury and the operation usually favorably influences the outcome and operations should be delayed until patients have at least considerably recovered from shock. Prolonged shock and hemorrhage produce irreversible deleterious effects and should be combated early. In the presence of considerable hemorrhage, transfusions during and shortly after operation totaling as much as 3,000 cc. of blood may be necessary. Transfusions should, whenever possible, displace the administration of saline, dextrose infusions or stimulant drugs. The ricochet of bullets and the position of the patient at the time of injury as compared with his position on the operating table accounts for apparently bizarre courses of bullets. Unexpected and unpredictable visceral injuries due to the position of the patient or the phase of respiration at the time of injury were observed frequently. Perforations of hollow

or solid viscera were only slightly less frequent among the patients who lived than among those who died. Extraperitoneal hemorrhage or hemorrhage between the leaves of the mesentery is likely to obscure important injuries. Drains introduced into the peritoneal cavity are undesirable, but drainage of the abdominal wall should be instituted when hollow viscera have been perforated. Silk or cotton sutures and ligatures are superior to catgut for the repair of hollow viscera and for the closure of the abdominal wall. Irrigation or lavage of the peritoneal cavity is usually futile, but it is desirable to suck out or pick out from the peritoneal cavity liquid blood, blood clots, detached particles of viscera, intestinal contents and foreign bodies. The avoidance of enemas and flushes aids in preventing or reducing the severity of ileus and peritonitis. Biologic preparations and chemotherapeutic agents may prove of value in reducing the mortality from peritonitis resulting from penetrating abdominal wounds. Lyophiled serum or whole blood transfusions are sometimes necessary to maintain plasma protein at a normal level postoperatively. Atelectasis and pneumonia are frequent complications. The mortality of the eleven cases of stab wounds was 27.2 per cent and of the thirty-five cases of gunshot wounds 40 per cent. Recent advances in the treatment of shock, hemorrhage, ileus and peritonitis should help in lowering this high mortality.

Surgical Management of Bile Duct Stones.—According to Allen and Wallace, from October 1930 to October 1935 1,228 patients were operated on in the Baker Memorial and the Massachusetts General hospitals for disease of the extrahepatic biliary system. Of these, 395 had exploration of the common bile duct, 231 had instrumentation of the papilla (with an average dilation of 7 mm.) and 164 had nothing more done than the removal of the calculi and the determination that the papilla was patent. From October 1935 to October 1939, 860 additional patients were subjected to operations. Of these, 380 had common duct exploration and 330 had their papillae dilated; only fifty had a simple exploration. It is, therefore, apparent that more of the staff have become convinced of the safety and rationale of routine, gentle and gradual dilation of the duct outlet. Such dilation does not increase the mortality. In fact, it would seem that the procedure is attended by less risk than exploration alone. It would seem that at least one of Bakes's claims may have been justified, i. e. dilation enhances the flow of bile into the duodenum. There were more postoperative pulmonary complications in the group that had had dilation of the papilla. Fatal bile peritonitis occurred in four of the patients who had dilation, while none occurred in the nondilated group. However, the authors believe that the technical difficulties of drainage accounting for these deaths have been corrected. There was a lower though not marked or significant percentage of mortality among patients who had dilation of the papilla. The nonfatal complications were greater in patients who did not have instrumentation of the papilla. They were evident in prolonged external bile drainage, increased hospital stay and secondary operations. Serious ascending infection did not follow instrumentation of the papilla. Duodenal reflux occurred in only one case, and this cleared up spontaneously. Late cicatricial constriction of the dilated papilla did not occur. The permanence of the dilation in the average case is doubted. In large ducts dilated to 1 cm. the sphincteric action may be lost. Under these circumstances, the health of the patient was not interfered with.

Acute Pancreatitis.—Morton and Widger feel that it is unfortunate to limit the blood amylase test to a transient period in the severe hemorrhagic necrotic forms of pancreatitis. They suggest that blood should be taken for blood matching for transfusion, for the icteric index and for the amylase test. If perforated ulcer or obstruction is suspected roentgenograms may demonstrate free air in the abdominal cavity or they may show the obstructed loops. If these examinations reveal nothing significant, the amylase test may be helpful in arriving at the correct diagnosis. Abdominal paracentesis may be of assistance. An amylase test on fluid recovered by aspiration may be diagnostic. In the authors' cases in which the pancreas was drained the fluid gave high amylase test values. Acute pancreatic abscesses should be drained. The acute, fulminating, hemorrhagic, necrotic type has had a high mortality rate in the past from immediate operation. Shock should be adequately treated and fluid balance restored in these cases. In the very ill patients the most simple surgical treatment should be undertaken. If jaundice is present, drainage of the gallbladder or common duct may be advantageous. The pancreas should be disturbed as little as possible, as it cannot be drained by splitting the capsule as formerly advocated. The drains should be placed against the surface of the pancreas after the peritoneum over it has been spread apart or incised. In the milder edematous form of acute pancreatitis the amylase test is most useful. This form of pancreatitis subsides in most instances. After the subsidence exploration of the common duct with drainage for some weeks is usually all that is necessary for cure.

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Staphylococcic Infections of Kidney.—Nesbit and Dick state that certain features of acute staphylococcic infections of the kidney tend to obscure its early diagnosis. The condition is frequently not recognized and its complications—perinephric abscess and renal carbuncle—are rarely diagnosed until they have been present for some time. Eighty such cases seen at the University Hospital are discussed. The cases presented no apparent preexisting infection of the urinary tract and were uncomplicated by obstructive lesions. The route of infection is hematogenous. Staphylococcus aureus is the most frequent invading organism, although any of the other strains of staphylococcus may be responsible. The port of entry is the skin or mucous membranes. Furuncles and carbuncles are the most common cutaneous foci, while infections of the upper respiratory tract are the most frequent mucosal precursors. In many instances no primary lesion can be demonstrated, suggesting that the port of bacterial invasion may be insignificant. The kidney is enlarged and multiple small areas of suppuration are disseminated throughout the cortex. The more extensive suppurative processes, which occur rarely, have been described as "abscess of the kidney," "septic infarct" and "renal carbuncle." The lesions heal rapidly unless extensive suppuration occurs. In all but seven of the eighty cases the onset was abrupt. Costovertebral pain of moderate severity, constant and aching, was present from the onset in all but three. If extremely severe, it simulated renal colic. Loss of appetite, malaise, general weakness, occasionally prostration and rarely nausea and vomiting were present. Chills occurred in forty-six. The average temperature was 102 F. Leukocytosis was constant. Staphylococci are demonstrated in the urine by staining the centrifuged sediment. Their rapid disappearance has often led to confusion in diagnosis not only of simple coccic renal infection but also of its serious complications. Secondary invasion by the colon bacillus occurred from the seventh to the tenth day and persisted longer than the primary invader in twenty-nine of the eighty cases. With this invasion pus cells always appeared in the urine. The diagnosis is made without difficulty, except in rare instances in which the urine fails to show cocci for the first few days. In these cases costovertebral tenderness, fever and leukocytosis are diagnostic. Failure of diagnosis is generally due to failure to suspect the disease. The lesion most commonly confused with this condition is acute appendicitis, but the absence of nausea, vomiting and muscle spasm, with the presence of costovertebral tenderness and high leukocytosis, should be sufficient for differentiation. Acute hydronephrosis and cholecystitis must be ruled out. Uncomplicated staphylococcic renal infections run a stormy course the first week, followed by improvement of all symptoms and signs. Usually by the fourteenth day the temperature returns to normal and the patient is free from pain or tenderness. If symptoms and signs fail to subside or are accentuated, one of the surgical complications must be suspected. Uncomplicated cases end in complete recovery, except for cortical scars, which probably have no bearing on renal function. Patients with surprisingly serious infections without complications recover quite rapidly without operation. The nine patients with renal carbuncle were treated by operation; nephrectomy was performed on one and simple drainage on the others, with eventual complete healing in each instance. The forty-eight patients with perinephric abscess were all treated by incision and drainage. There were no postoperative deaths and no secondary nephrectomies. All pulmonary complications of renal or perirenal suppuration cleared up promptly on adequate surgical drainage of the subdiaphragmatic primary lesion.

Pelvic Lavage with Sulfanilamide for Renal Infections.—Austen administered sulfanilamide directly to ten patients with infections of the upper part of the urinary tract. These patients either did not tolerate the drug well or it was unwise to administer it by the usual routes because of anemia, granulocytopenia, diminished renal function, or the presence of an anatomic or pathologic abnormality preventing high local concentration or because there was interference with renal drainage. The drug administered by direct pelvic instillation was well tolerated by all except one patient. A definite clinical and bacteriologic improvement was observed in eight cases, a bacteriologic cure in one and no improvement in one. Observations on the concentration of sulfanilamide in the blood, in the urine from the injected kidney and in the urine from the uninjected kidney demonstrated that the drug was absorbed from the renal pelvis into the blood stream in appreciable amounts and that it was also excreted in the urine from the uninjected kidney. The concentration of sulfanilamide in the urine from the injected kidney reaches a much higher level than is possible when the drug is administered by the oral or subcutaneous routes. The author feels that although the method has definite limitations the direct pelvic instillation of sulfanilamide is a worth while procedure in the treatment of selected cases of renal infection.

Treatment of Gonorrheal Arthritis.—Culp evaluates the efficacy of various therapeutic measures employed at the Johns Hopkins Hospital in the treatment of gonorrheal arthritis during the last twenty years. The unimpaired function of the joint as the end result was the chief criterion used. Only those cases in which there was no doubt about the true etiology of the arthritis were included. They have been unselected otherwise. Forty-five of the cases were chronic, fifty subacute and 105 acute. Of the methods employed, sulfanilamide, intravenous injections of mercurochrome and fever therapy gave the best results. Of twenty-nine patients treated with intravenous injections of mercurochrome 69 per cent were discharged as being

well or markedly improved. Excellent results were obtained in cases of chronic, subacute and acute involvement. Only 53 per cent of the nineteen patients given fever therapy were well or markedly improved. Most of these were given only one session of fever. Several patients had severe reactions, and one died while undergoing treatment. Cures were effected in the chronic as well as in the earlier cases. Of the twenty-two patients treated with sulfanilamide 68 per cent left the hospital well or markedly improved. Most of the cases were acute and showed amazing improvement despite bone changes in a few instances. Results were less striking in cases of subacute and chronic involvement. Chemotherapy appears to be more efficacious than any other treatment. Sulfanilamide and intravenous injections of mercurochrome are recommended for the routine treatment of gonorrheal arthritis and seem to be of about equal therapeutic value. Both often result in surprisingly rapid cures. The thirty-four patients whose treatment was limited to bed rest and sedatives did poorly. Baking, diathermy, massage, prostatic massage and passive motion failed to cure any of the forty-nine patients. Poor results were obtained in the remaining forty-one cases with aspiration and the injection of air, hot compresses, manipulation under anesthesia, immobilization, incision and drainage or vaccines (typhoid or antigonococcus).

Kentucky Medical Journal, Bowling Green

38:187-230 (May) 1940

Newer Concepts of Allergy. M. B. Cohen, Cleveland.—p. 188.
Diagnosis of Allergic Conditions. F. A. Simon, Louisville.—p. 190.
Treatment of More Common Allergic Diseases. A. E. Cohen, Louisville.—p. 193.
Allergy in Dermatology. A. B. Loveman, Louisville.—p. 195.
The Management of the Allergic Child. I. Rosenbaum Jr., Louisville.—p. 199.
Treatment of Pneumonia in Children with Sulfapyridine. W. W. Nicholson, Louisville.—p. 203.
Rupture of Urinary Bladder. N. L. Bosworth, Lexington.—p. 206.
Differential Diagnosis of Acute Exanthems. C. C. Carroll, White Mills.—p. 209.
Hemorrhoids: Local and Systemic Considerations. R. C. Alley, Lexington.—p. 212.
Etiology and Management of Posterior Position. W. Hord, Maysville.—p. 215.
Swine Erysipelas in Man. D. L. Jones, Fulton.—p. 218.
Anemia as a Problem for the Pediatrician. H. Gordon, Louisville.—p. 222.
Tuberculous Meningitis: Report of Case. H. G. Wells, Georgetown.—p. 224.

Medical Annals of District of Columbia, Washington

9:153-188 (May) 1940

Sulfapyridine: Its Nature and Some Theories of Its Action. G. B. Roth, Washington.—p. 153.
Clinical Use of Sulfathiazole in Pneumonia. T. J. Abernethy, Washington.—p. 159.
"Vascular Headache": Report of Case Successfully Treated with Histamine. W. M. Yater, Washington.—p. 165.
The New Law for the Commitment of the Mentally Ill. R. S. Cohen, Washington.—p. 167.
Granuloma Resulting from Penetration of Talcum Powder: Report of Case. E. de Savitsch, Washington.—p. 169.

Minnesota Medicine, St. Paul

23:311-382 (May) 1940

*Gastroscopic Observations in Pernicious Anemia. J. B. Carey, Minneapolis.—p. 311.
Proper and Adequate Protein Diet for Elderly People. E. L. Tuohy, Duluth.—p. 313.
Genital Tuberculosis. G. J. Thomas, T. L. Stebbins, Minneapolis, and F. J. Rigos, Oak Terrace.—p. 318.
Surgical Drainage of Abdomen: Review of Literature. R. A. Glabe, Plainview.—p. 323.
Management of Acute Abdominal Emergencies. J. M. Waugh, Rochester.—p. 331.
Treatment of Mental Defectives in Minnesota. E. J. Engberg, Faribault.—p. 335.
Present Day Treatment of Ununited Fractures of Neck of Femur. M. S. Henderson, Rochester.—p. 339.
Surgery of Common and Hepatic Duct Calculi. H. Mattson, Minneapolis.—p. 344.
*Fulminating Ulcerative Colitis: Critical Analysis of Twenty Cases. C. P. Schlicke and J. A. Bargen, Rochester.—p. 348.

Gastroscopic Observations in Pernicious Anemia.—According to Carey, many patients with pernicious anemia have been examined gastroscopically and the presence of an atrophy of greater or lesser degree has been noted. Whether this condition is amenable to adequate liver therapy has been discussed, and favorable and unfavorable results have been recorded. The author has not seen an indubitable case of pernicious anemia with a normal gastric mucosa in the course of 750 examinations. He has not seen restoration to a normal condition of the gastric mucosa in any of the patients reexamined after treatment, although in some cases some evidence of regeneration was present. Of fifteen patients in whom the diagnosis of pernicious anemia had been made on the basis of all the accepted criteria, six were reexamined and still showed atrophic mucosa, although in two there was some improvement in that there were present what were thought to be areas of regeneration. One was definitely worse in that the atrophy was more extensive, and three were unchanged. The author points out that the reversion to a normal condition of the gastric mucosa in pernicious anemia patients treated with liver would be contrary to the pathologic and histologic studies of Meulengracht and Faber. Both of these authors have examined postmortem material from pernicious anemia patients adequately controlled as to anemia and dying from intercurrent causes and have always found an atrophic condition of the mucosa with gastritis. Changed conditions of general nutrition and blood elements brought about by liver therapy might conceivably result in some improvement in gross appearance of gastric mucosa as to color and even in the direction of recession of atrophic appearance. But in any gastritis the replacement of diseased gastric cells is by nonspecific, simple columnar epithelium and not by functional cells capable of secreting specific substances. This is in line with the experimental evidence that the hydrochloric acid does not return to the gastric secretion in pernicious anemia in spontaneous or induced remission, nor does the so-called intrinsic factor. If liver therapy actually restored the gastric mucosa to normal, the patient would be actually cured of his pernicious anemia. This happy result has, so far, not been accomplished.

Fulminating Ulcerative Colitis.—Schlicke and Bargen state that approximately 300 cases of chronic ulcerative colitis have been seen at the Mayo Clinic during each of the last three years and that between five and seven patients have died from this disease annually. The cases selected for study represent the last ten in which the outcome was fatal. As a basis for comparison, an analysis was made of ten similar cases of fulminating ulcerative colitis, in which the patient recovered. This investigation represents an attempt to make a critical analysis of the factors contributing toward the mortality and of the value of the therapeutic efforts with an attempt to improve the management of similar cases in the future. Most of the patients were in the third or fourth decade of life. Nine of the twenty patients were Jews. The severity of the disease and the outcome bore no relation to the duration of the symptoms, the mode of onset, the type or extent of involvement of the colon at the time of admission or to the blood picture. The similarity in the course of the two groups of cases is emphasized by the fact that in each there were seven cases presenting severe sepsis and two or three presenting secondary deficiency states. Streptococci of colitis were recovered from the stools in all but one case in which the patient survived but in only two of the cases in which the patient died. In most cases the clinical picture and course were produced or, at least, influenced by the severity of the infective process, but in some a secondary deficiency state was the predominant feature. Perforation, jaundice and edema were the most serious complications. Perforation and peritonitis were the most common causes of death. No one drug or procedure is curative in "chronic ulcerative colitis" of this fulminating variety. A program including the use of serums and vaccine and embracing dietary and medicinal aids seems to be the best form of treatment. Each of the ten patients who survived received an adequate course of serum. Few of the ten who died received amounts of serum worthy of comment. Nine of the patients who survived received anticolitis vaccine as well. Only two of the patients who died received the vaccine. The use of sulfanilamide and azosulfamide in the treatment of chronic ulcerative colitis is still in a trial stage. Although of proved value in many cases, their use is not entirely unattended by danger, especially in cases of the fulminating variety.

New England Journal of Medicine, Boston

222:783-826 (May 9) 1940

Acute Appendicitis as Complication of Carcinoma of Cecum. M. K. Bartlett and R. H. Miller, Boston.—p. 783.
The National Health Act of 1939. R. B. Osgood, Boston.—p. 785.
*Prognostic Factors in Carcinoma of Breast. G. W. Taylor and N. H. Bruce, Boston.—p. 790.
*Antemortem Recognition of Pulmonary Embolism. A. S. Johnson, Springfield, Mass.—p. 793.
Otolaryngology. C. G. Flake, Boston.—p. 796.

222:827-864 (May 16) 1940

Fractures of Carpal Scaphoid. A. Thorndike Jr. and W. E. Garrey, Boston.—p. 827.
Changes in Public Health Practice. C. F. Wilinsky, Boston.—p. 831.
Fever Therapy in Allergic Disease. R. W. Hyde, Fairfax, Vt.—p. 839.

Prognostic Factors in Carcinoma of Breast.—According to Taylor and Bruce, in a considerable number of cases of carcinoma of the breast, operable by the usual criteria and subjected to radical mastectomy, early recurrence of the disease develops and runs a rapidly fatal course. In an effort to discover factors common to these cases and possibly of prognostic value, the authors have studied a group of thirty patients, all of whom had received radical mastectomy, with subsequent rapid recurrence and death within eighteen months. For comparison, two other similarly treated groups were studied. One of these consisted of forty-eight patients who had died of recurrence after eighteen months, while the other was made up of forty-seven patients living and well five or more years after the radical mastectomy. These groups were investigated with regard to such factors as preoperative duration, size and location of lesion, cutaneous involvement and axillary involvement. The preoperative duration was shorter and the size of the lesion smaller in cured cases. Large lesions and those with cutaneous involvement or extensive axillary involvement offer a poor prognosis, in many cases so poor as to contraindicate surgical intervention even in the absence of remote metastases. The operative risk must be given careful consideration. Old age, obesity and hypertension seem to increase the hazard. While it is still impossible to prognosticate accurately in any single borderline case, the authors believe that the chance of cure should be carefully weighed against the operative risk and the normal life expectancy. Palliative measures may well be indicated more often than they are now employed.

Antemortem Recognition of Pulmonary Embolism.—Johnson thinks that the unanimity of opinion as to the diagnostic criteria for pulmonary embolism should render an accurate diagnosis a simple matter. A study of forty-three fatal cases in which necropsy showed pulmonary embolism to have been the immediate cause of death revealed that only three cases answered the description of pulmonary embolism. In nine cases the clinical picture was so atypical as to make the diagnosis of pulmonary embolism unwarranted, even in retrospect. Furthermore, the author encountered a significant number of patients who presented a sufficient number of these criteria ante mortem to warrant a diagnosis of pulmonary embolism but in whom the pathologist found sepsis, without evidence of embolism, as the cause of death. This study was undertaken in order to reappraise the validity of accepted diagnostic criteria. The author reviews observations on the forty-three cases and compares them with those of other investigators. He presents histories of nine cases in which the picture was so bizarre that a clinical diagnosis of fatal pulmonary embolism seemed unjustified. Before any lifesaving form of therapy can be instituted the clinical diagnosis of pulmonary embolism must be made. In about two thirds of the fatal cases the patients survive long enough for the application of some remedial measure. The author emphasizes the frequency and seriousness of pulmonary embolism and suggests that its possibility should be considered in any case in which the patient is not doing well, even though he has undergone no operation and presents no signs of infection. Dyspnea, tachycardia and cyanosis are early and frequent signs. Although often accompanied by collapse, this feature may be absent or may occur alone. There appears to be no single criterion short of necropsy by which the diagnosis of pulmonary embolism can be infallibly established or excluded. It is believed, however, that if it is remembered that this condition can mimic, and be mimicked by, coronary thrombosis, bronchopneumonia, sepsis and surgical shock, greater diagnostic acumen will be developed.

New York State Journal of Medicine, New York

40:693-762 (May 1) 1940

Cesarean Section: Ten Year Study Conducted in Rochester and Monroe County by the Committee on Maternal Welfare of the Medical Society of the County of Monroe. J. K. Quigley, Rochester.—p. 699.
Role of Infection in Sudden Death. J. R. Lisa and J. F. Hart, New York.—p. 705.
Preliminary Report on Activated Ergosterol: Form of High Dosage Vitamin D in Treatment of Chronic Arthritis. R. G. Snyder and W. H. Squires, New York.—p. 708.
Clinical Report on Eye Lesions Due to Nasal Sinus Infection. F. Barber and J. J. McNamara, Rochester.—p. 720.
Dermatitis Nodularis Necrotica: Report of Three Cases. E. T. Bernstein, New York.—p. 727.
Benign Intraventricular Tumors of Brain: Report of Three Cases. E. Campbell Jr. and R. Whitfield, Albany.—p. 733.
Milk: Role of Medical Milk Commissions in Developing Standards for Milk Production. E. S. Rimer, New York.—p. 741.
*Toxic Manifestations of Sulfapyridine. S. Katz, Newark, N. J.—p. 746.

Toxic Manifestations of Sulfapyridine.—Katz studied 100 consecutive patients for toxic manifestations of sulfapyridine. All symptoms and signs referable to toxicity were carefully recorded. Approximately one half of the adults and one fifth of the children exhibited some toxic side reactions. Nausea and vomiting, appearing in 25 per cent, were the most commonly encountered toxic manifestations. There was no apparent correlation between the gastric irritability and the amount of the drug administered. Disturbances of the central nervous system were observed in 7 per cent and varied from mild personality changes to the more serious psychoses. There were four cases of hematuria. This disturbance is apparently caused by the irritating effect of the sharp acetylsulfapyridine crystals that precipitate in the urine. Stasis appears to be an important predisposing factor in the production of hematuria following the use of sulfapyridine. Dermatitis in two cases and jaundice in three were the other serious symptoms noted. Diarrhea, lethargy, abdominal pain, cyanosis and dyspnea were also encountered. Drug fever, vertigo, headache, tingling of the extremities, acute hemolytic anemia and granulocytopenia were not observed. With the recognition of the toxic manifestations constant observation will allow detection of the toxic symptoms while they are amenable to appropiate countermeasures permitting this valuable drug to be used with a satisfactory margin of safety.

40:763-836 (May 15) 1940

Biliary Duct Stones. P. Vayo and L. F. Simpson, Rochester.—p. 769.
Infections of Neck. A. G. Swift, Syracuse.—p. 779.
*Carcinoma of Breast. L. C. Kress, W. T. Murphy and E. M. Burke, Buffalo.—p. 787.
The New York Diabetic Association: Summer Camp for Underprivileged Diabetic Children. F. W. Williams and J. F. Hart, New York.—p. 795.
Postcaval Ureter. F. O. Harbach, Syracuse.—p. 800.
Use of Calcium Chloride in Treatment of Chills. P. B. Beeson and C. L. Hoagland, New York.—p. 803.
Pathology of Experimentally Produced Pulmonary Tuberculosis in Rabbit: Effect of Prophylactic Vaccination. E. M. Medlar and K. T. Sasano, Mount McGregor.—p. 805.
Toxemias of Pregnancy. M. B. Strauss, Boston.—p. 810.

Carcinoma of Breast.—Kress and his associates present their impressions gained over a period of four years from a study of 129 patients with cancer of the breast who received preoperative irradiation. All these tumors were proved malignant by aspiration biopsy, by careful removal of a small piece of the tumor or by operation. Preoperative irradiation was not instituted until a definite diagnosis was made. None of the patients were less than 30 years of age; the predominating age group was between 40 to 70. Carcinomas were equally frequent in the two breasts. The most common site was the upper outer quadrant of the breast. A lump was the principal first symptom and pain was next. Most of the lumps were discovered by the patient. The physician does not have the opportunity to detect early cancer, as patients do not generally have periodic health examinations. Delay from the discovery of the first symptom to medical consultation averaged 9.28 months. Popular cancer education is the solution for this delay.

The value of preoperative irradiation is questionable. It cannot replace surgery. Preoperative irradiation rendered 19 per cent of the tumors sterile. Very few axillary glands were sterilized by preoperative irradiation. Swelling of the arm and delayed union were encountered more often when preoperative irradiation was used. The most suitable interval between irradiation and surgery is eight weeks. The large cell tumor was found to be more sensitive to irradiation, the small cell was the least, and the sensitivity of the adenocarcinoma lay between these two groups.

Oklahoma State Medical Assn. Journal, Oklahoma City

33:1-58 (May) 1940

Renal Tumors of the Wilms Type. H. S. Browne, Tulsa.—p. 6.
Use of Vitallium Screws in Fractures of Long Bones. F. A. Stuart, Tulsa.—p. 8.
Some Recent Advances in Ophthalmology. J. R. Reed, Oklahoma City.—p. 12.
Résumé of Advance Made in Treatment of Human Pellagra, with Observation Made on Fifty Cases Treated with Nicotinic Acid and Whole Yeast Compounds. V. H. Musick, Oklahoma City.—p. 13.
Anesthesia and Analgesia in Obstetrics and Its Relation to Asphyxia Neonatorum. R. J. Reichert, Moore.—p. 17.

Pennsylvania Medical Journal, Harrisburg

43:1057-1248 (May) 1940

Relationship of Urticaria and Angioneurotic Edema to General Medicine. W. L. Winkenwerder, Baltimore.—p. 1073.
Acrosclerosis. L. Hollander and H. R. Vogel, Pittsburgh.—p. 1089.
Spreading Peritonitis: Its Prevention and Treatment. W. W. Babcock, Philadelphia.—p. 1093.
*Use of Sulfanilamide in Treatment of Peritonitis of Appendical Origin. I. S. Ravdin, J. S. Lockwood and J. E. Rhoads, Philadelphia.—p. 1100.
Surgical Treatment of Dislocated Lens. W. S. Reese, Philadelphia.—p. 1104.
Salt and Water Balance and Acid-Base Equilibrium: Body Water and Electrolyte Control: General Application. C. G. Grosscup, Abington.—p. 1106.
Id.: In Renal Disease. G. M. Piersol, Philadelphia.—p. 1111.
Id.: The Problem of Water Balance in Congestive Heart Failure. W. D. Stroud and J. B. Vander Veer, Philadelphia.—p. 1116.
Id.: Surgical Applications of Principles of Salt and Water Balance. D. B. Pfeiffer, Philadelphia.—p. 1121.
Complicating Factors Following Open Reduction of Simple Fractures. D. C. Geist, Philadelphia.—p. 1126.
Acute Laryngotracheobronchitis. F. W. Davison, Danville.—p. 1129.
Lung Abscess. H. A. Kipp, Pittsburgh.—p. 1134.
Pollen Asthma and Hay Fever in Children. S. C. Copeland and J. P. Keating, Philadelphia.—p. 1137.
Progress Report from Division of Cancer Control of the Department of Health of the Commonwealth of Pennsylvania. S. P. Reimann, Philadelphia.—p. 1141.

Sulfanilamide for Peritonitis of Appendical Origin.—Ravdin and his associates point out that the mortality among 552 patients operated on for acute appendicitis with abscess or acute appendicitis with peritonitis prior to 1936 was 1.4 per cent. This includes one patient, nearly moribund on admission, who was not operated on. In this group are included only those patients with a pathologic report of acute diffuse suppurative appendicitis or worse. In 1936 the authors added the parenteral administration of sulfanilamide to their regular regimen. Since then and up to Sept. 1, 1939, 286 patients with acute appendicitis and acute appendicitis with abscess or varying degrees of peritonitis have been operated on, with a mortality of 0.3 per cent. The only death which occurred was of a patient who had an acutely inflamed appendix but little evidence of peritonitis. Sulfanilamide was begun two days after operation when evidences of a widespread peritoneal infection were apparent. Necropsy disclosed a leaking appendical stump. Although the reduction in mortality does not appear to be great, the authors are convinced that a number of lives of desperately sick patients have been saved by the administration of sulfanilamide during the postoperative period. Drainage is necessary in many instances. It has been used in 38 per cent of the 838 cases. The McBurney incision permits the placing of drains in contact with the parietal peritoneum so that intestinal obstruction is minimized. Ileostomy has been necessary only once since the routine use of suction drainage in 1933. In nearly every instance the sulfanilamide has been given by hypodermoclysis. The crystalline sulfanilamide (Merck) was used. It was used preoperatively in cases of appendical abscess so as to minimize spread of the infection if transperitoneal drainage became necessary. The total dosage given has been approximately 8 Gm. the first day, the amount being gradually reduced to 3 Gm. in from four to six days, at which time if the patient was doing well the drug was discontinued. The daily dosage is given in from four to six doses. The blood concentration of sulfanilamide has been maintained above 5 mg. per hundred cubic centimeters of blood, and in a few cases it was kept above 15 mg. Drug therapy was continued in all instances until peristalsis was reestablished, flatus was passed by the anus, abdominal relaxation had taken place and the temperature and pulse rate were returning to normal. No accessory method of treatment can take the place of early operation and skilful surgery, but late operation is often necessary and it is in such cases of desperate illness that accessory therapeutic agents can help reduce the mortality.

Public Health Reports, Washington, D. C.

55:861-914 (May 17) 1940

Duration of Illness from Specific Diseases Among 9,000 Families, Based on Nationwide Periodic Canvasses, 1928-1931. S. D. Collins.—p. 861.
Some Developments in Water Pollution Research Program of the Public Health Service. J. K. Hoskins.—p. 893.
Viability of Aedes Aegypti Eggs. J. H. Le Van.—p. 900.

Radiology, Syracuse, N. Y.

34:521-650 (May) 1940

Tuberculous Hilar and Mediastinal Adenopathy in Adults. B. P. Widmann, H. W. Ostrum and J. S. Fetter, Philadelphia.—p. 521.
Intractable Heartburn of Pregnancy. J. R. Evans and J. S. Bouslog, Denver.—p. 530.
Why the Film Size? R. A. Rendich and L. A. Harrington, Brooklyn.—p. 536.
Irradiation and Hereditary Mammary Cancer. S. E. Owen and A. E. Williams, Hines, Ill.—p. 541.
Ileocecal Region. A. Oppenheimer, Beirut, Lebanon, Syria.—p. 545.
Radium Protection: Measurements of Exposure to Gamma Rays. R. E. Fricke and M. M. D. Williams, Rochester, Minn.—p. 560.
Cholecystography: Optimal Voltage: Tetrabromphenolphthalein versus Tetraiodophenolphthalein. R. R. Newell and R. Briggs, San Francisco.—p. 568.
Protrusion of Appendical Stump Following Appendectomy. M. Feldman, Baltimore.—p. 571.
Odontomas: Case Report. L. A. Malone, Terre Haute, Ind.—p. 573.
Multiple Diverticula of Jejunum, Duodenum and Colon: Report of Case. S. Hatchette, Lake Charles, La.—p. 577.
Recent Advances in Nuclear Physics. E. U. Condon, Pittsburgh.—p. 581.
Lower Lobe Tuberculosis. M. J. Sokoloff, Philadelphia.—p. 589.
*Group X-Ray Surveys in Apparently Healthy Individuals. A. B. Robins and D. E. Ehrlich, New York.—p. 595.
Treatment of Carcinoma of Rectum by Electrocoagulation and Radiation in Selected Cases. H. I. Teperson, Brooklyn.—p. 610.
Shellac Bezoars. H. H. Inlow, Shelbyville, Ind.—p. 618.
Serial Planeography (Serioscopy) and Serial Planigraphy: Critical Analysis. J. Kaufman and H. Koster, Brooklyn.—p. 626.

Group X-Ray Surveys.—Robins and Ehrlich report the result of examining more than 73,000 apparently healthy individuals roentgenographed in a routine manner from January 1937 to September 1938. There were 14,177 high school children, 53,237 persons of the home relief population of Harlem, 3,643 homeless men and 2,500 prisoners committed for not longer than three years. Active tuberculosis was found in 0.4 per cent of the high school children. The incidence of 3.1 per cent of active pulmonary tuberculosis in the home relief population is in close agreement with results previously obtained in New York City. The highest incidence of active tuberculosis was obtained in the prisoners, 5.9 per cent of them showing significant lesions. Since the prison sentence of this population was short, the high rate of disease is to be attributed to the economic background and is not associated with the stay in the penal institution. Confirmatory evidence of the importance of economic status and its attendant living conditions on tuberculosis is evidenced by the 16.1 per cent incidence among the homeless men. The average age of this group of men was 50 years and they existed at a bare subsistence level. The tuberculosis of more than 5 per cent of these men was active. The incidence of active and arrested tuberculosis by age followed the expected pattern. The distribution of active pulmonary tuberculosis by age and sex closely paralleled the mortality curves for men and women in New York City. Contrary to accepted beliefs, the incidence of active tuberculosis in the Negro population of the groups was considerably lower than in the

white population. Only in the high school group was the rate in Negroes higher than in the white population. Most of the cases in the entire group were discovered in the minimal stage of tuberculosis. Abnormal cardiac outlines significant of organic disease of the heart or vessels were found in a sufficiently high percentage of cases to warrant the universal use of roentgenography. In rapid examinations of large groups, the roll-paper method is the procedure of choice from the point of view of convenience, accuracy and economy.

Southern Medical Journal, Birmingham, Ala.

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*Local Implantation of Sulfanilamide in Compound Fractures: Its Effect on Healing. J. A. Key and T. H. Burford, St. Louis.—p. 449.
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Chronic Leg Ulcerations in Congenital Hemolytic Jaundice. L. H. Leger and T. G. Orr, Kansas City, Kan.—p. 463.
Chronic Female Pelvic Disease. R. J. Wilkinson, Huntington, W. Va.—p. 464.
*Familial Benign Chronic Pemphigus: Report of Thirteen Cases in Four Generations of a Family and Report of Nine Additional Cases in Four Generations of a Family. Howard Hailey and Hugh Hailey, Atlanta, Ga.—p. 477.
Roentgenologic Aid in Acute Infections of Lung and Their Sequelae. H. B. Mulholland, University, Va.—p. 482.
*Prolonged Atelectasis of Both Foreign Body and Nonforeign Body Origin: Bronchiectasis as End Result and Its Prevention by Bronchoscopic Care. V. K. Hart, Charlotte, N. C.—p. 487.
Glaucoma Errors That I Have Made and That I Have Seen. H. S. Gradle, Chicago.—p. 498.
Thyroid Anesthesia: Comparative Study. H. E. Doudna and G. S. Mechling, Oklahoma City.—p. 502.
Public Health Aspects of the Trichinosis Problem in the South. K. B. Kerr, Washington, D. C.—p. 511.
Prophylaxis of Malaria. H. Beckman, Milwaukee.—p. 516.
Acute Anterior Poliomyelitis in South Carolina in 1939. W. Weston Jr., Columbia, S. C.—p. 525.
Method for Initiating Respiration in the Newborn. N. Bograd, Montgomery, Ala.—p. 531.

Local Implantation of Sulfanilamide in Compound Fractures.—Key and Burford determined the effect of local implantation of crystals of sulfanilamide in experimental contaminated fracture wounds in rabbits and dogs. They found that such implantation did not retard the union of the experimental fracture of one foreleg when compared with the degree of union present in a similar fracture in the other foreleg. Local implantation of sulfanilamide crystals in compound fractures not only tends to lessen the danger of infection but does not perceptibly interfere with the union of the soft tissues or of the bone. However, such implantation does not permit the closing of grossly contaminated or infected wounds. The wound must be debrided in the usual way and all foreign material and devitalized tissue removed before the infection has gained a foothold and invaded the tissues, preferably within twelve hours after the injury. After the débridement and reduction of the fracture, the skin and subcutaneous tissues are sutured with a single layer of silkworm gut without drainage in order to retain the serum which is saturated with sulfanilamide. The authors believe that postoperative immobilization is an important factor in the prevention of infection. The upper limits of the method are not known but its routine use will enable the average surgeon to close with impunity most compound fractures. This is important not only in civil life but even more so in military surgery. Had the casualty wounds during the war of 1914-1918 been rapidly debrided, sprinkled with sulfanilamide crystals, sutured and the reduced fractures immobilized in casts or splints, the large majority of them would have stayed closed without infection and the soldiers could have been sent directly back to America from the casualty clearing station or field hospital. The method would have brought about a great saving in hospital personnel and materials and the effect on the morale of the soldiers would have been unlimited. The method is recommended in clean operations in which the development of an infection is feared; that is, operations involving tissues previously infected and in which the infection apparently has disappeared. Good results have also been obtained in the wounds of amputation stumps when the operation was done for gangrene and infection.

Familial Benign Chronic Pemphigus.—The Haileys add twenty-two cases of familial benign chronic pemphigus to their four previously reported cases. The cases occurred in four generations of two families. The disease is familial and hereditary but not congenital. It is most likely to appear in early adult life and follow a chronic course over a period of years, with frequent recurrences and varying periods of freedom from the eruption. Toward late life the severity and frequency of the attacks are reduced. The disease is benign. There are no constitutional signs and symptoms and the disease does not appear to shorten the span of life. Pruritus or burning may be present. Tender regional lymph nodes are not constant. The primary lesion is a vesicle or a bulla arising on apparently normal skin. Nikolsky's sign (the skin is easily rubbed off) is present. Temporary pigmentation marks the site of recently healed lesions. Scarring never occurs. The lesions have a predilection for the neck, flexures and apposing cutaneous surfaces. Mucous membranes may be attacked. Treatment does not influence the course of the disease. Mild antiseptic wet dressings in the moist and early stage of the disease are palliative and discourage secondary infection. Boric acid ointment with 1 per cent ammoniated mercury on gauze makes a soothing dressing for the dry stage of the eruption. The authors state that their first report of the condition is substantiated by the present work. A number of authorities have observed similar cases and agree that another dermatologic entity, familial benign chronic pemphigus, has been identified.

Prolonged Atelectasis.—Hart emphasizes that prolonged atelectasis is the frequent forerunner of bronchiectasis. Therefore adequate drainage, particularly by bronchoscopy, is important. Nearly all bronchiectasis is acquired, much of it in childhood. Congenital bronchiectasis is rare. A congenital atelectasis is more probable with a subsequent bronchiectasis. There is increasing clinical and experimental evidence that atelectasis is the preceding and predisposing cause of bronchiectasis. The duration of atelectasis regardless of cause before bronchoscopic drainage is undertaken determines the rapidity of cure and the degree of future bronchiectasis. The sooner bronchoscopic care is undertaken, the greater the rapidity of cure and the number of recoveries. Conversely, the longer bronchoscopy is deferred the smaller the number of recoveries and the possibility of bronchiectasis as an end result is increased. Bronchiectasis is assumed to date from some acute illness of the respiratory tract with obstruction and infection as the dominant factors. Three things may happen: resolution without chronic changes, acute bronchiectasis or a potential bronchiectatic condition. The latter, if unchecked, may progress successively to early or more advanced cylindrical or saccular bronchiectasis or a combination of the two. Once bronchiectasis is established there is no cure but radical surgery, and this can be done only in selected cases. This further emphasizes the importance of prophylactic bronchoscopic care. The author purposely limits his case reports to children. Together with other bronchoscopists, he feels that this group represents the largest and most fertile field for prophylactic bronchoscopic care. Typical atelectasis is occasionally produced by abnormal tissue in the bronchus. In a child, this is usually not malignant and in the absence of a foreign body is probably most commonly produced by the erosion of the bronchial wall by a tuberculous lymyh node, with the production of granulation tissue. The same may occur in an adult. Early bronchoscopic removal is definitely indicated. A healed bronchial stricture should likewise be treated bronchoscopically by dilatation if obstruction and atelectasis ensue.

Tennessee State Medical Assn. Journal, Nashville

33:159-196 (May) 1940

An American Health Program. N. B. Van Etten, New York.—p. 159.
Why Medicine? W. O. Baird, Henderson.—p. 168.

Wisconsin Medical Journal, Madison

39:337-412 (May) 1940

Adequate Dietary in Later Life. E. L. Tuohy, Duluth, Minn.—p. 353.
Observations on Use of Sulfapyridine. T. E. Gundersen, La Crosse, and M. Friedman, Kansas City, Mo.—p. 360.
Persistent Enuresis. A. J. Hood and B. B. Madison, Milwaukee.—p. 363.
Thrombophlebitis in Obstetrics. A. M. Lindner, Racine.—p. 368.
Nonsuppurative Disease of Cornea. E. R. Ryan, Milwaukee.—p. 372.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Dermatology and Syphilis, London

52:141-172 (May) 1940

Cancer of Skin. H. MacCormac.—p. 141.
Dermatitis from 9-Bromofluorene and Peculiar Reaction to Patch Test: Case. A. Cavendish.—p. 155.

British Journal of Ophthalmology, London

24:201-264 (May) 1940

The Fundus and Fovea Centralis of Albatross (Diomedea Cauta Cauta—Gould). K. O'Day.—p. 201.
Spasm of Branch of Central Artery: Personal Experience. H. Grimsdale.—p. 208.
Mycetoma of Eyelid. J. S. Aldridge and R. Kirk.—p. 211.
Development of Ophthalmology in Bombay. J. N. Duggan and V. K. Chitnis.—p. 213.
Microphthalmia and Visual Pathways: Case Associated with Blindness and Imbecility, and Sex Linked. S. E. Whitnall and R. M. Norman.—p. 229.

British Medical Journal, London

1:757-798 (May 11) 1940

Recent Knowledge of Incidence and Control of Cerebrospinal Fever. E. A. Underwood.—p. 757.
Goiter in South Wales. I. J. Davies and L. Rogers.—p. 764.
Renal Threshold for Glucose: Normal and in Diabetics. R. D. Lawrence.—p. 766.
Prevention of Throat Infection. Helen Pixell Goodrich and G. L. Way.—p. 768.
*Congenital Complete Heart Block: Effect of Atropine: Case. G. M. Currie.—p. 769.

Congenital Complete Heart Block.—Currie reports a case of congenital complete heart block in a child of 2 admitted to the hospital with a probable diagnosis of meningitis or infantile convulsions. X-ray examination revealed enlargement of the heart due to congenital abnormality. Electrocardiograms, before and after the injection of atropine, showed that the drug failed to break the complete block. The effect of 1/100 grain (0.00065 Gm.) of atropine was to raise the auricular rate out of all proportion to the rise in the ventricular rate; the latter fell much more quickly to its original rate than the auricular. Electrocardiograms eight months later still showed a complete block, the auricular rate being 124 a minute and the ventricular rate 36. Since the previous examination the parents, now instructed as to what to look for, had been able to describe several Stokes-Adams attacks, lasting a few minutes at the most. Otherwise the child had been well and had played about normally. The case is one in which atropine affected the ventricular rate in spite of the complete block cutting off action through nerve control. On another occasion, after the injection of 3 minims (0.2 cc.) of epinephrine the ventricular rate rose to 48, the block still remaining complete. In view of the clinical observations, the compliance with Yater's postulates, the x-ray study and the electrocardiograms, this is undoubtedly a case of congenital complete heart block, associated with probable patent interventricular septum and Stokes-Adams attacks.

Indian Medical Gazette, Calcutta

75:129-192 (March) 1940

Aortic Stenosis. G. Kelly.—p. 129.
*Observations on Use of Nicotinic Acid in Treatment of Pellagra and Allied Conditions. J. W. D. Goodall.—p. 147.
Experience with Diseases of Gallbladder. V. M. Kaikini.—p. 153.
Adult of Microfilaria Malayi Brug, 1927. S. Sundar Rao and P. A. Maplestone.—p. 159.
Simple and Inexpensive Flea-Proof Cage. C. L. Pasricha and G. Panja.—p. 160.
Topical Application of Sulfanilamides. A. C. Dey.—p. 161.

Nicotinic Acid for Pellagra and Allied Conditions.—Goodall used nicotinic acid in the treatment of three cases of true pellagra, twelve of nicotinic acid deficiency and miscellaneous cases of allied conditions. Nicotinic acid was given in varying dosages according to the severity of the case. Of the twenty patients, eleven were cured, seven were improved, one did not finish the course of treatment and one obtained no improvement. The author states that although pellagra is quite a common disease in Bengal there is a much larger group of cases of nicotinic acid deficiency, especially among Anglo-Indians, showing such symptoms as sore tongue, anorexia, stomatitis, diarrhea and mental dulness, which respond well to nicotinic acid therapy. Certain cutaneous conditions, such as infected scabies, show improvement with nicotinic acid therapy because this medication increases the blood supply of the affected area.

75:193-256 (April) 1940. **Partial Index**

Comparison of Thymol and Some Other Drugs in Treatment of Hookworm Infection. P. A. Maplestone and A. K. Mukerji.—p. 193.
Haffkinine (Acriquine), an Atabrine-like Compound Prepared in India, in Indian Strains of Malaria. R. N. Chopra, R. T. M. Hayter and B. Sen.—p. 200.
Crinodora (Palusan) in Indian Strains of Malaria. R. N. Chopra, R. T. M. Hayter, B. Sen and M. Talukdar.—p. 202.
Typhus Fever in Bombay. T. B. Patel.—p. 208.
Miniature Mass Radiography (Plea for Its Adoption). S. C. Roy.—p. 209.
Role of X-Ray Screening in Detecting Pulmonary Tuberculosis. K. Eisenstaedt and A. U. Rindani.—p. 210.
Destruction of Air-Borne Bacteria. R. C. Wats and G. K. Kamat.—p. 212.
Role of Calcid Fumigation as Raticidal and Pulicidal Measure in Anti-plague Campaign. C. L. Ahluwalia.—p. 219.
Note on Production of Agglutinins in Blood of Individuals After Peroral and Subcutaneous Vaccination by Typhoid and Paratyphoid Vaccines. E. Somasekhar.—p. 223.

Journal of Mental Science, London

86:341-590 (May) 1940

Morgagni's Syndrome: Clinical and Pathologic Study. R. E. Hemphill and E. Stengel.—p. 341.
Contribution of Rorschach Method to Wartime Psychologic Problems. M. R. Harrower-Erickson.—p. 366.
Prognosis in Schizophrenia. D. Blair.—p. 378.
Adaptiveness and Equilibrium. W. R. Ashby.—p. 478.
Has Fear Any Therapeutic Significance in Convulsion Therapy? L. C. Cook.—p. 484.
Some Observations on Psychologic Aspects of Cardiazol Therapy. R. Good.—p. 491.
Influence of Cardiazol on Chronic Schizophrenia. A. J. Bain.—p. 502.
Relationship Between Disturbance of Liver Function and Mental Disease. P. Berkenau.—p. 514.
Prolonged Narcosis with Paraldehyde and Dial. M. B. Brody.—p. 526.
Note on Use of the 1937 Revision of Stanford Binet Vocabulary List in Mental Hospital Patients. M. B. Brody.—p. 532.
Ascorbic Acid Levels in Patients Suffering from Psychoses of Senium. D. G. Remp, S. R. Rosen, J. B. Ziegler and D. E. Cameron.—p. 534.

Lancet, London

1:865-910 (May 11) 1940

Laboratory Diagnosis of Diphtheria: Comparative Values of Various Mediums. K. E. Cooper, F. C. Happold, K. I. Johnstone, J. W. McLeod, H. E. de C. Woodcock and K. S. Zinnemann.—p. 865.
Death in the First Month and the First Year. C. McNeil.—p. 869.
*Follicular Hyperkeratosis: Sign of Malnutrition? J. Pemberton.—p. 871.
Hypertensive Effect of Blood from Hypertensive Dogs. D. Y. Solandt, R. Nassim and C. R. Cowan.—p. 873.
Spontaneous Pneumothorax and Staphylococcic Lung Abscess in an Infant. J. L. Collis and A. F. Foster-Carter.—p. 875.
Removal of Impacted Lower Wisdom Tooth. W. W. James.—p. 876.
Treatment of Dropsy with Mercurial Diuretics and Urea. M. Winternitz.—p. 879.

Follicular Hyperkeratosis.—The cutaneous eruption described by Pemberton was observed during a survey of the nutrition of adolescents, school children and children of preschool age in different parts of Great Britain. The eruption consists of crops of enlarged hair follicles appearing first on the extensor aspects of the arms, legs and buttocks and later and less commonly over the scapulas, back and abdomen. The eruption is symmetrical and does not irritate. The skin feels dry and rough and is sometimes furfuraceous. The hair follicles are enlarged, firm and cone shaped. The hair is absent from many follicles, and in its place there projects a tiny spine of horny material. These spines account for the roughness or "nutmeg-grater skin." At the orifices of some of the follicles the hair can still be seen, often curled, shriveled or broken. Occasionally the follicle is mildly inflamed. Sometimes the enlarged follicle is surmounted by a flat imbricated scale instead of a horny spine. The sexes were equally affected but it was not seen in children under 5. The fully developed condition was present in about 5 per cent of 3,000 children. Simple enlargement of the hair follicles, resembling a permanent cutis anserina, on the extensor aspects of the arms and legs, without projection of horny spines from the orifices of the follicles, was

found in about 20 per cent of the children. In these cases the skin was not noticeably dry. The eruption tends to develop in several members of the same family. Microscopic examination showed hyperkeratosis of the hair follicles, absence of sebaceous glands and round cell infiltration round the follicles. It is thought that this eruption is similar to the follicular hyperkeratosis or phrynoderma described by various writers in Africa and the Far East and that it is of nutritional origin. The specific dietary deficiency to which follicular hyperkeratosis may be attributed has not been certainly established, but the condition is probably an early sign of a deficiency of vitamin A or of fat.

New Zealand Medical Journal, Wellington

39:63-116 (April) 1940

*X-Ray Treatment of Carcinoma of Breast: Survey of Results. B. Mackenzie.—p. 66.
Goiter After Middle Age. R. Chisholm.—p. 74.
Physiologic Approach to Study of Hysteria. I. M. Allen.—p. 79.
Catheterization of Ejaculatory Ducts. C. M. Greenslade.—p. 88.
Conservative Surgical Treatment of Acute Salpingitis: Report of Two Cases. R. O'Regan.—p. 93.

Roentgen Treatment of Carcinoma of Breast.—Mackenzie treated 104 cases of mammary cancer from private practice with x-rays. A high proportion of these were advanced with postoperative metastases or with inoperable primary lesions, and many were referred for only palliative treatment. Forty-nine patients (47 per cent) are still living. The period of survival ranges from three months to sixteen years, with an average of 5.4 years from the initial symptom. The five year survival rate is 35 per cent dating from roentgen therapy and 47 per cent dating from operation, the difference being due to the time lapse between operation and roentgen treatment. The average duration of life among the dead was 3.5 years calculated from the date of operation and 2.1 years from roentgen treatment. The prognosis appears to be better when the interval between operation and roentgen treatment is short. The value of ovarian irradiation in premenopausal established breast cancer is shown. In women before the menopause the results of this treatment are frequently dramatic. Advanced multiple metastases in bone, lung and skin (and possibly elsewhere) may clinically disappear without any local treatment to the metastases. This disappearance is hastened by small local doses of radiation. The period of freedom from symptoms is much longer than after only local treatment and survivals of five and six years are now on record. In women past the menopause the prognosis is little if at all improved by ovarian irradiation. The inferences to be drawn are that there is a natural tendency for breast cancer cells to revert to nonmalignant tissues and that, on the assumption that x-rays act inhibitively, this tendency is prevented directly or indirectly by the presence in the system of a substance elaborated by the ovary. At the normal menopause the elaboration of this substance would appear to be taken over by other tissues, thus accounting for the absence of postmenopausal response to ovarian irradiation. A questionnaire addressed to nearly 200 women whom the author has treated with ovarian irradiation for menorrhagia and nonmalignant conditions in the last eighteen years has revealed only one case in which breast cancer has developed. The numbers are too small to base conclusions, but they support the contention that the incidence of breast cancer is less after ovarian irradiation. Because of the strikingly favorable influence on demonstrable gross metastases, the author advises artificial sterilization of all women with breast cancer before the menopause. Inhibition of ovarian activity has no demonstrable effect on cancers of other organs, with the possible exception of the uterus, where the satisfactory results of roentgen therapy may in part be accounted for by the results of ovarian irradiation.

Chinese Medical Journal, Peiping

57:201-300 (March) 1940

Massive Amyloidosis of Both Adrenal Cortices: Clinical Syndrome with Pathologic Findings. I. Snapper and K. Y. Ch'in.—p. 201.
Quantitative Determination of Urinary Estrogens in Cases of Uterine Hemorrhage. Hazel Ai-Ch'ün Lin.—p. 216.
Transplantation of Established External Biliary Fistula into Duodenum: Report of Case. C. K. Chi.—p. 231.
Acute Monocytic Leukemia: Report of Two Cases in Chinese. H. T. Hsiang.—p. 240.
Chinese Anthelmintic Prescriptions: Examples from the Han Period to the Present Time. C. S. Chao.—p. 251.

Bruxelles-Médical, Brussels

20:717-743 (April 14) 1940

*Typhus Fever. M. Gaud and A. Pocoule.—p. 717.
Two Cases of Uteroplacental Apoplexy Treated Medicinally. R. De Guchteneere.—p. 724.
Placenta Praevia Accreta Discovered During Cesarean Section for Placenta Praevia: Subtotal Hysterectomy. R. Schockaert.—p. 729.

Typhus Fever.—Gaud and Pocoule report the epidemiologic observations made in Northern Africa on typhus fever and the successful use of a vaccine virus prepared in the Pasteur Institute of Morocco by G. Blanc and his collaborators. They attribute the endemic and epidemic recrudescences of typhus fever to the viability of the virus in the excreta of infected lice deposited on garments and thus easily transmitted, especially in times of economic distress entailing congestion and migrations. Mouse virus in fecal deposits of fleas kept dry was found to retain its virulence even after 300 days, a dose of 0.01 mg. causing infection. The vaccine recovered from fleas infected with mouse typhus and then emulsified was successful in more than 1,500,000 cases, elicited benign sequels (in only 3 per cent of the natives inoculated) and caused no deaths. Clinically the involvement of the reticulo-endothelial system is significant in typhus. Meteorologic factors may be implicated in the cyclic recurrence of the disease.

Schweizerische medizinische Wochenschrift, Basel

70:337-364 (April 20) 1940. **Partial Index**

Sulfanilamidothiazole: Contribution to Chemotherapy of Coccic Infections. M. Hartmann.—p. 337.
Id.: New Chemotherapeutics of the Sulfanilamide Series. R. Meier, O. Allemann and E. Merz.—p. 338.
Chemotherapy of Acute Infectious Diseases by Means of Sulfanilamidothiazole. O. Gsell.—p. 342.
*Comparative Clinical and Necropsy Studies of Bone Marrow. H. Jeanneret.—p. 351.
Gynecomastia with Obesity and Constitutional Acromegaloid Hypertrophy, Syndrome of Hyperfunction of Anterior Pituitary. M. Schachter.—p. 357.

Necropsy Study of Bone Marrow.—Jeanneret made microscopic examinations of bone marrow in fifty-eight cases coming to necropsy. Several aspirations were made in each case by means of a sternal puncture, the first specimen being taken during the first hour after death, the others at short intervals. The cadaveric bone marrow, withdrawn less than an hour after death and examined as a stained smear, is comparable to the marrow of the living subject in cellular sharpness; it is slightly inferior in affinity to the May-Grünwald-Giemsa stain. Postmortem alteration of the medullary elements appears in from one to three hours. It involves first the polymorphonuclear neutrophils and somewhat later the myelocytes. The nucleus of the normoblast undergoes pyknosis and fragmentation. The plasmocytes, lymphocytes and stroma cells change slowly, as do also the eosinophils. Myelocytic or erythroblastic mitosis, as well as the thrombocytes, disappears in one or two hours. The myelogram is greatly modified. The proportion of polymorphonuclears decreases rapidly, falling to zero in from eight to twenty-four hours; that of the myelocytes and of the cells of the stroma appears to increase. These processes depend only slightly on the ambient temperature, but septic conditions accelerate them greatly. Accurate study of bone marrow is possible during the three hours immediately following death; this interval is reduced by one hour and a half in the case of acute purulent infection. An anatomic diagnosis of granulocytopenia or of plasmocytoma is possible for twelve hours. It is the same with the estimation of the hemopoietic activity from the number of erythroblasts. In ten of the fifty-eight necropsies the author followed every sternal puncture by a costotomy. The medullary contents of the costal fragment were immediately pressed out and smeared on a slide. The costal marrow differs perceptibly from the sternal marrow; in the first, the proportion of stroma cells and of myelocytes as well as the quantity of fat are much greater; in the second the polymorphonuclears predominate. The author supposes that during the sternal puncture a sorting takes place among the cellular elements. The ripe cells are carried away in great numbers, whereas the less mobile young forms as well as the better fixed cells of the stroma are not. A sternal puncture may thus give an incorrect picture of the state of the hemopoietic organs. The myelogram, accord-

ing to the terminology of Arneth, will be much deviated "toward the right" and thus approach the hemogram. Sternal puncture made immediately after death will provide accurate information as to the proportion of the different elements. The author believes that necropsy is valuable in clarifying numerous unsolved problems of the bone marrow and its functions.

Chirurgia degli Organi di Movimento, Bologna

25:287-442 (April) 1940. **Partial Index**

Modern Trends in Treatment of Congenital Luxation of Hip Joint. O. Scaglietti.—p. 308.
*Circumscribed Cortical Osteitis. M. Paltrinieri.—p. 407.

Circumscribed Cortical Osteitis.—Paltrinieri reports nineteen cases of circumscribed cortical diaphysial osteitis, a condition as frequent as Brodie's abscess but not well understood. It was a late complication of osteomyelitis and was caused by staphylococcus. The author found that it generally develops in childhood or during the prepuberal age. The tibia, femur and humerus are the bones most frequently involved. The most constant sign is the cyclic appearance of dull pain by night, which disappears after from two to four hours. The cortical focus shows on x-ray examination a small round zone of rarefaction, limited by thickness of the cortical portions of the diaphysis. The medullary cavity is normal. The lesion is a cavity of from 0.5 to 1 cm. in diameter, containing variable purulent material, thick pus, necrotic osseous tissue, a small sequestrum and granulation tissue. The periosteal reaction is like that of sclerosis in chronic osteitis. The disease is chronic. The treatment consists in removal of the osteitic focus followed by immobilization or of opening of the focus, draining and immobilization.

Policlinico, Rome

47:125-168 (April 15) 1940. **Surgical Section**

*Treatment of Acute Cholecystitis of Typhoid. F. Benedetti Valentini.—p. 125.
Intussusception of Cecal Haustra: Cases. E. Sovena.—p. 142.

Treatment of Acute Cholecystitis of Typhoid.—According to Benedetti Valentini, acute cholecystitis in the course of typhoid or during convalescence is grave and calls for early surgical intervention of cholecystostomy with drainage. The operation controls local inflammation, prevents perforation, stimulates elimination of biliary calculi (which as a rule are present in such cases) and of bile contaminated by typhoid bacilli. In acute cases it is advisable to suture the gallbladder to the parietal peritoneum under a local anesthesia and to perform a cholecystostomy with drainage three or four days later. Early cholecystostomy gives better results than cholecystectomy. The acute condition was controlled in two grave cases out of five reported by the author and a recovery was obtained. Cholecystectomy performed after perforation in three cases failed to save the patients.

Prensa Médica Argentina, Buenos Aires

27:905-956 (May 1) 1940. **Partial Index**

*Ascorbic Acid in Cerebrospinal Fluid. M. Castex and M. Schteingart.—p. 905.
Quinine Salts Treatment of Hearing Hallucinations. J. C. Vivaldo and A. Barrancos.—p. 938.

Ascorbic Acid in Cerebrospinal Fluid.—Castex and Schteingart made quantitative determinations of the ascorbic acid content in the cerebrospinal fluid, either normal or altered from disease of the central nervous system, of fifty-nine adults ranging in age from 16 to 70, and likewise in the cerebrospinal fluid, blood and urine of ten patients of this group. The amount of ascorbic acid averaged 0.0027 Gm. for each hundred cubic centimeters of normal cerebrospinal fluid, and 0.0021 Gm. for each hundred cubic centimeters of pathologic cerebrospinal fluid. The figures for ascorbic acid in the normal fluid were higher than those in the blood and the urine of the same patients and were independent of one another. There was no relationship between the age and the amount of ascorbic acid in the normal cerebrospinal fluid. The quantitative variations of ascorbic acid in the cerebrospinal fluid in diseases of the central nervous system were inconstant and not related to the disease or to the alterations of the fluid. Simple quantitative determination of ascorbic acid in the cerebrospinal fluid is of no diagnostic value in determining hypovitaminosis C, as the figures may be normal in the presence of vitamin C inadequacy. The determination of ascorbic acid in the blood and urine after ingestion of vitamin C (administration of vitamin C for from eight to ten consecutive days up to a total dose of from 0.3 to 0.5 Gm. of the substance) is a reliable clinical test for the diagnosis of hypovitaminosis C.

Deutsche Zeitschrift für Nervenheilkunde, Berlin

150:97-192 (March 21) 1940. **Partial Index**

Craniostenosis and Craniodysostosis. A. Mandel.—p. 105.
"Inflammatory Polyneuritis." W. Noell.—p. 119.
Pathogenesis of Foci in Multiple Sclerosis. G. Döring.—p. 146.
*Sequels After Head Injuries with Special Consideration of "Traumatogenic General Cerebral Syndrome." H. Saethre.—p. 163.
Rare Metencephalitic Respiratory Disturbance: Contribution to Problem of Respiratory Movement. H. Plügge and A. J. Anthony.—p. 176.

Sequels After Head Injuries.—The material reviewed by Saethre consists of 574 patients with 589 injuries; 258 were early and 316 late cases. The importance of alcoholism is demonstrated by the fact that in 30 per cent of the new cases the patient was under the influence of alcohol when brought to the hospital and that one third of the patients with traumatic psychosis were chronic alcoholic addicts. The syndrome of commotio cerebri existed in 67.5 per cent of the head injuries. Loss of consciousness persisted in three fourths of the cases for less than two hours. Of those in which loss of consciousness persisted for more than twenty-four hours only six presented the pure syndrome of commotio cerebri. Neurologic disturbances were observed in 54.7 per cent of the new cases and in 35 per cent of the late cases. In more than half of the late cases otologic symptoms predominated. Olfactory paresthesias and anosmia were likewise relatively frequent. Traumatic epilepsy was observed in 5 per cent. The author regards it as inadvisable to apply the term "traumatic neurosis" to the subjective symptoms of patients with head injuries; he thinks that this term should be restricted to cases in which intracranial lesions are absent. He suggests that the subjective symptoms be classified into (1) the traumatogenic cerebral general syndrome (headaches, vertigo and difficulties in thinking) and (2) psychogenic symptoms (*a*) primary, those due to shock and (*b*) secondary, the psychoreactive and compensatory symptoms. The traumatogenic cerebral general syndrome predominated in 49.4 per cent of the cases, the psychogenic symptoms in 24.8 per cent and the organic neurologic symptoms in 25.77 per cent.

Medizinische Klinik, Berlin

36:341-368 (March 29) 1940. **Partial Index**

Erection of Vertebral Fractures According to Böhler. J. C. Lehmann.—p. 341.
*Etiology and Early Recognition of Congenital Dislocation of Hip Joint. H. Storck.—p. 342.
*Coxa Vara, Its Cause and Treatment. P. Pitzen.—p. 344.
Technic of Plaster of Paris Cast. W. Birkenfeld.—p. 347.
Bronchial Carcinoma. J. Wätjen.—p. 349.
Trauma and Pathogenesis of Cancer. B. Ostertag and G. Mundt.—p. 351.
Influence of Blood Transfusion on Hematopoiesis in Bone Marrow. H. Wildegans and Helga Kröning.—p. 353.

Congenital Dislocation of Hip Joint.—Storck believes that deviations in the shape of the uterus, which, like twin pregnancies, are dependent on hereditary factors, establish an endogenic element, which, by deviation in the position of the fetus, elicits constrained spatial conditions causing luxation of the hip and torticollis. Since twin pregnancy is hereditarily transmitted also in the male line, the possibility cannot be denied that breech position (considered as a rudimentary twin pregnancy) and the deformities caused thereby can be transmitted by the male line. Thus dislocation of the hip could be considered as a secondary manifestation which has only an indirect connection with hereditary twin pregnancy. For the practitioner these observations suggest the necessity of careful observation of children, particularly girls, born in breech presentation. Special attention should be given to disturbances in the hip joint. Inhibition of straddling, difference in the length of the legs and asymmetries in the region of the pelvic bone may be the precursors of a dislocation of the hip joint.

Coxa Vara, Its Cause and Treatment.—According to Pitzen, congenital coxa vara develops probably on the basis of endochondral congenital disturbances in ossification. The roent-

genogram discloses a structural defect which runs from the center of the epiphysial line vertically, or slightly laterally downward through the neck of the femur, so that together with the epiphysial line it forms an upside-down Y. This defect is not really congenital, but develops later under the influence of the stress of weight. For this reason, the designation "congenital" has been rejected by some in favor of the term coxa vara "infantum." The cause of rachitic coxa vara is evident. The coxa vara of adolescence is the result of local osteomalacia of the cervical metaphysis of the femur, which in turn causes backward and downward sliding of the head of the femur. The osteomalacic process develops probably on the basis of an endocrine disorder, because it appears generally in patients with adiposogenital dystrophia or with eunuchoid gigantism. Trauma is as a rule merely an intensifying factor in coxa vara of adolescents. The treatment is determined by the cause and the nature of the coxa vara. General treatment produces results in rachitic coxa vara only. With the disappearance of rickets under antirachitic therapy the deformities of the neck of the femur disappear as a rule.

Monatsschrift für Kinderheilkunde, Berlin

82:1-132 (March 8) 1940. **Partial Index**

Use of Urine of Convalescent Patients for Mitigation of Acute Infectious Diseases. M. Krebs.—p. 1.
Treatment of Nephrosis in Childhood. Ilse Schmidt.—p. 9.
Pertussis and Tuberculosis. Ickert.—p. 15.
Effect of Vitamin B_1 on Postdiphtheritic Paralysis. J. Dieckhoff.—p. 53.
*Atypical Adult Rickets Suggesting "Dysostosis Enchondralis Metaphysaria," Cured by Single Dose of Vitamin D_3: Case. E. Hassler.—p. 63.

Atypical Late Rickets.—Hassler reports the case of a prematurely born girl, now aged 6½ years, of normal mentality who had been intensively managed against rickets since her third year. When she was 4 years old, rachitic symptoms appeared in different parts of the skeletal system, especially in the distal portion of the right leg, involving talipes. Progressive deterioration caused her to be hospitalized. The laboratory tests (x-ray examination, microscopy of excised bone, blood analysis) disclosed normal processes of calcification, with extensive proliferation of connective tissue, normal phosphorus and calcium levels of the blood serum and a pathologic picture that suggested "dysostosis enchondralis metaphysaria." An inspiration prompted the author to administer a massive dose of 7.5 mg. of vitamin D_3. The child was seen again eight months later and showed a complete recovery. Skeletal modifications were scarcely noticeable in the roentgenograms.

Nervenarzt, Berlin

13:97-144 (March) 1940. **Partial Index**

Cerebral Malformations and Epilepsy. A. Bannwarth.—p. 97.
*Verification of Value of Laignel-Lavastine and Koressios' Hemolytic Serum in Treatment of Multiple Sclerosis. P. Beck and P. Martini.—p. 103.
Hereditability of Amyotrophic Lateral Sclerosis. R. Dittel.—p. 121.
Diagnostic Difficulties in Bürger's Disease of Brain: Case. V. Schretzenmayr.—p. 124.

Hemolytic Serum in Multiple Sclerosis.—Beck and Martini, instructed in the technic by Koressios, employed the hemolytic serum named after Laignel-Lavastine and Koressios in forty-six cases of multiple sclerosis and report observations strikingly at variance with the successful results recently claimed by the French originators of the serum (a rabbit serum treated with blood derived from patients with multiple sclerosis). All forty-six cases save one were either of recent origin (seven) or of somewhat less recent development (thirty-eight). Twelve had been under observation for one and a half years, nineteen for from one and a half to two years and fifteen for more than two years. Dosage, consisting initially of 0.5 cc. of the serum, had been increased under proper control when deemed necessary. In thirty-one cases no change in the gravity or course of the disease was noted; seven showed temporary or subjective signs of improvement but ultimately had to be classed with the failures. Several of the early cases were observed to grow worse in the course of the treatment. Thirty-nine of the forty-six cases are regarded as furnishing negative results. The authors' skepticism of the favorable results obtained by the French authors is based on a more rigorous conception of what constitutes improvement. In view of the well known variable manifestations in multiple sclerosis and the frequency of remissions, subjective ameliorations, they think, viewed against a background of unmodified objective symptoms, need to be cautiously interpreted. Even the more recent significance attached to the serum by Koressios as "group specific" for infectious diseases of the nervous system, because it evoked prolonged and extensive cutaneous reactions in multiple sclerosis and in various forms of encephalitis, is challenged by the clinical reviewers. They were able to duplicate the same reactions by means of a hemolytic rabbit serum treated with the blood of normal persons.

Zeitschrift f. d. ges. experimentelle Medizin, Berlin

107:321-466 (Feb. 19) 1940. **Partial Index**

Hemothorax. H. Bauer.—p. 321.
Extrahepatic Function of Bilirubin in Exudates and Hematomas. K. Dirr and E. Klemm.—p. 338.
*Lipase Level of Blood Serum. H. Hangleiter and A. Reuter.—p. 355.
Effects of Partial Baths on Temperature of Skin. G. Riemerschmid and O. Scheurer.—p. 373.
*Has Dysfunction of Lipoid Metabolism a Specific Significance for Malignant Tumors? K. Dirr and E. Sommer.—p. 393.

Lipase Level of Blood Serum.—Hangleiter and Reuter examined 150 serums of normal controls and of patients presenting a variety of diseases by means of a modified tributyrin method in order to determine the lipase content of the blood serum. In cases of diabetes mellitus the level was generally within the lower normal limits. In cases of carcinoma and in those of liver and of gallbladder diseases the level was greatly diminished. No typical changes were observed in cases of gastritis, enteritis, pneumonia and other infectious diseases, with the exception of those of tuberculosis, in which the lipase level was low. In cases of multiple sclerosis approximately normal lipase values were found. However, the paucity of cases did not justify conclusions on the connection between lipase levels and the pathogenesis of the disease. Further tests with ingestion of food rich in fats and with an intubation procedure conveying enzymes such as pestled pancreone in large quantities directly into the duodenum failed to augment the lipase level of the blood stream. Histamine, however, was effective in increasing lipolytic fermentation.

Dysfunction of Lipoid Metabolism in Malignant Tumors.—Dirr and Sommer examined the diagnostic validity of Ascoli's view that the serums of persons with malignant tumors possess lipoids with abundant unsaturated valences not found in normal or in other pathologic serums. By dividing the total of unsaturated valences with these labile unsaturated valences, called "disposable," Ascoli found a general quotient of 6, the relative relations between total and "disposable" valences never varying. However, in the serums of persons with malignant tumors Ascoli found a quotient of 2 to 3, attributing this change to an increase in "disposable" valences. Dirr and Sommer, testing Ascoli's method and results in a group of seventeen normal and nonlipoid labile controls, twenty-four lipoid labile persons and fourteen patients with malignant tumors, were able to confirm Ascoli's view that serums of patients with malignant tumors show an increase in the number of disposable, unsaturated valences. However, they found not an absolute but only a relative increase compared with the total valence count, the total count fluctuating strongly. They, therefore, conclude that lipoid metabolic dysfunction is nonspecific for malignant tumors and that further investigations are needed.

Zeitschrift f. menschliche Vererbungslehre, Berlin

24:161-264 (March 12) 1940

*Hereditary Implications in Allergic Diseases. K. G. Horneck.—p. 161.
Caries and Paradentosis in Twins. G. Nehls.—p. 235.
Relation of Constitutional Type to Class Attainments of College Seniors. G. Just and W. Kramaschke.—p. 248.

Hereditary Implications in Allergic Diseases.—Horneck investigated the history of 1,280 unselected persons, belonging to 519 families and twenty-five family groups, for a hereditary background of allergic, associated (begleitkrankheiten) and neuropathic diseases. (The term associated diseases is used to include acute rheumatic arthritis, arthritis deformans, muscular rheumatism, gout, biliary and renal calculus, ulcus ventriculi

and duodeni.) In 278 persons (21.7 per cent), of whom 116 were children, allergic manifestations either existed or had existed; associated diseases were represented in 156 and neuropathic involvements in 102. In eighty-three cases an allergy had been observed during the first decade of life, predominating among the male patients. In puberty, allergies in females gained the ascendancy and retained it until the seventeenth year (26 per cent in females against 2.9 per cent in males); thereafter allergic incipiency was at a minimum. Significant allergies in female subjects consisted especially of migraine, hay fever, Quincke's edema and eczema. In adults bronchial asthma, hay fever and eczema occurred in the ratio of 10 per cent in men to 6.8 per cent in women. Unskilled labor was represented forty-eight times (20.7 per cent) in the allergic picture, skilled labor and artisans thirty-seven times (22 per cent), white collar workers such as clerks, petty officials and small tradesmen forty-nine times (22.1 per cent) and the professions twenty-three times. Allergic diseases were twice as common among urban (11.9 per cent) as among rural dwellers (4.3 per cent). Successive generations of the same family presented either the same allergy or allergic variations. Pathologic connections were directly traceable to the parents in 175 cases (62.2 per cent). Siblings of allergic persons showed no increased incidence rate in allergic and associated diseases compared with the rate of the general population, but siblings of neuropathic persons or of those with associated diseases did show an increase in allergy manifestations. Five times as many neuropathic conditions were found among allergic persons as among nonallergic—fifty-eight out of 278 (20.8 per cent) against forty-four out of 1,002 (4.4 per cent)—justifying the assumption that neuropathic conditions constitute a nutrient soil for allergic diseases. Leptosomatic and asthenic constitutional types were observed to possess a susceptibility to migraine, to acute rheumatic arthritis and to ulcus ventriculi and duodeni, whereas the pyknic and muscular type was inclined to bronchial asthma, Quincke's edema, gelosis, muscular rheumatism, arthritis deformans and biliary and renal calculus. The incidence of allergic diseases in professional family groups showed a high elevation, about 30 per cent.

Eksperimentalna Meditsina, Kharkov

1-96 (No. 1) 1940. **Partial Index**

Biochemistry of Epinephrine and Adrenologenous System. A. M. Utevskiy and V. O. Osinska.—p. 1.
Proteolysis and Aminogenesis of Hepatic and Pulmonary Tissue in Sensitization and Anaphylactic Shock. L. S. Lifshits.—p. 6.
Quantitative and Qualitative Alterations of Pancreatic Secretion: Result of Painful Irritation. S. Ya. Yaroslav and E. B. Lakezhevskiy.—p. 13.
*Methylene Blue Disinfection of Conserved Blood. E. O. Spivak and I. A. Pelishenko.—p. 21.
Determination of Water in Biologic Tests. V. G. Gurevich and L. E. Carlson.—p. 28.

Sterilization of Conserved Blood with Methylene Blue.—Spivak and Pelishenko demonstrated a definite sterilizing effect of solution of methylene blue in experiments on citrated donor's blood contaminated with Streptococcus, Staphylococcus, Micrococcus albus, Bacillus coli and Bacillus subtilis. Methylene blue added to the citrated blood in amounts not exceeding the therapeutic dosage, from 0.04 Gm. to 100 cc. of blood, did not alter the osmotic resistance of the red cells and did not accelerate the onset of hemolysis. Irradiation of the blood with ultraviolet rays and short waves did not enhance the disinfecting effect of methylene blue.

Sovetskiy Vrachebnyy Zhurnal, Leningrad

Feb. 29, 1940 (No. 2) Pp. 81-160. **Partial Index**

Gunshot Injuries of the Chest. A. V. Smirnov.—p. 81.
Prophylaxis and Therapy of Grip. D. M. Rossiyskiy.—p. 87.
Gonorrheal Arthritis. I. M. Porudominskiy.—p. 95.
*Evaluation of Therapy of Pulmonary Suppuration. I. V. Neymark.—p. 101.
Repercussive Anisocoria in Peripheral Nervous Lesions. N. E. Osokin and E. M. Dovgyallo.—p. 109.
*Hypertonic Solution of Sodium Chloride Therapy of Trichomonal Vaginitis. Y. L. Dozortseva and R. S. Lifshits.—p. 121.

Pulmonary Suppuration.—So far as treatment is concerned, there is no need, according to Neymark, to differentiate between gangrene and abscess of the lung. The belief that gangrene of the lung is caused by anaerobic micro-organisms while the abscess is caused by aerobic ones has been disproved. The microflora may be identical in the two conditions, since both are apparently stages of the suppurative process. The postoperative mortality rate of the various surgical clinics is rather high (32 and 58 per cent). Most surgeons advise waiting from six weeks to two months after the onset of the symptoms before resorting to surgical intervention. Evaluation of conservative methods based on an analysis of the author's seventy-four cases is as follows: 1. Arsphenamine may be tried in the presence of fusiform spirochetal infection. It is contraindicated in suppurations on a tuberculous basis because of the tendency to provoke hemoptysis and febrile reaction. 2. Roentgen therapy is contraindicated in chronic abscess associated with bronchiectasis. It provokes in these cases spitting of blood and sharp rises of temperature. 3. Intravenous administration of 20 per cent alcohol proved to have an undoubted favorable effect on the acute abscess. It does not provoke hemoptysis or raise the temperature. It is not effective in chronic suppuration. 4. Oral administration of capsules containing potassium permanganate had a favorable though transient effect on chronic abscess. 5. The best results were obtained from the combination of the alcohol and the permanganate therapy. This effect is probably due to the oxidizing of the pulmonary tissue, rendering the soil less favorable for the bacterial flora and to its direct though mild bactericidal effect.

Trichomonal Vaginitis.—Dozortseva and Lifshits treated 100 patients with trichomonal vaginitis with hypertonic solution of sodium chloride. The majority of the patients were aged from 21 to 35. Practically all presented on examination a granular colpitis with hyperemic mucosa, irritation of the external genitalia and local tenderness on vaginal examination. In about 50 per cent there was associated gynecologic disease. Smears revealed numerous cocci and many leukocytes. The p_H of the vaginal secretions in many of the cases was from 6 to 7. Apparently Trichomonas can live and multiply in weakly acid, neutral and alkaline mediums. The treatment consisted of a daily vaginal douche with 1 liter of a 25 per cent solution of sodium chloride (one glass of kitchen salt to a liter of water) at a temperature of 38 C. Discharge was controlled, as a rule, after five or six treatments, and the Trichomonas were no longer present after from ten to fifteen douches. Colpitis and vulvitis disappeared simultaneously. The p_H of the vaginal secretions rose in many instances to 5. While the method is effective, it does not guarantee against recurrence. The authors advise that the douches be continued for some time after the Trichomonas have disappeared from the discharges.

Vrachebnoe Delo, Kharkov

22:1-80 (No. 1) 1940. **Partial Index**

New Paths in Treatment and Prophylaxis of Myopic Chorioretinitis. V. P. Filatov.—p. 1.
Blood Sugar and Chloride Levels as Index of Physiologic Status. G. V. Folbort.—p. 5.
Symptomatology and Pathogenesis of Extracapillary Nephritis. F. I. Litvak and D. D. Zaydenberg.—p. 11.
Pathologic Alterations in Hypophysis in Renal Disease. B. P. Kucherenko.—p. 31.
Roentgen Diagnosis of Malignant Tumors of the Kidney. M. M. Vaysfligel.—p. 37.
*Ultraviolet Irradiation in Grip. S. E. Vitebskiy.—p. 47.

Ultraviolet Irradiation in Grip.—Vitebskiy reports the effects of ultraviolet irradiation in 625 cases of grip observed during the epidemic of 1935-1936. The treatment was begun on the first day of sickness in 308 cases, on the second in 170, on the third in 112 and on the fourth in thirty-five. It consisted of a daily suberythemal dose of ultraviolet rays to the anterior and the posterior surfaces of the thorax. The minimal number of exposures was three and the maximal six. The temperature fell to normal after the first exposure in 55 per cent of the first group, after two exposures in 33 per cent and after three exposures in 12 per cent. In cases in which the treatment was begun on the second day of illness, the temperature came down to normal after one exposure in 51 per cent, after two exposures in 30 per cent and after three exposures in 19 per cent. In cases in which the treatment was begun on the third and the fourth day, the temperature came down to normal after the first exposure in 17 per cent, after the second in 30 per

cent and after the third and fourth in 53 per cent. It is thus apparent that the earlier the treatment was begun the quicker was the return of the temperature to normal. Along with the lowering of the temperature there was noted improvement in the subjective and the objective symptoms. The number of sick days in instances in which the treatment was begun on the first or second day amounted to three, which is from one and a half to two times less than in cases in which irradiation was not given. A favorable effect was likewise noted on diffuse postgripal bronchitis in a group of forty cases in which the treatment was begun on the third or the fourth day. The treatment here was extended to from six to ten exposures. There was not a single instance of bronchopneumonia or any other complication.

Geneeskundig Tijdschr. v. Nederl.-Indië, Batavia

80:917-988 (April 9) 1940

Secondary Glaucoma in Presence of Anterior Synechia. A. W. M. Houwer.—p. 918.
Tattooing of Corneal Leukomas with Candle Soot. A. W. M. Houwer.—p. 927.
*Xerophthalmia Among Children in Batavia. J. H. de Haas, J. H. Posthuma and O. Meulemans.—p. 928.
Operations for Cataract and Treatment of Xerophthalmia in the Netherland East Indies. J. Tijssen.—p. 951.

Xerophthalmia Among Children in Batavia.—According to de Haas and his collaborators, 259, or nearly 5 per cent, of the children admitted to the Central Civil Hospital in Batavia during the period from 1935 to 1938 had xerophthalmia. More than 40 per cent of these children were either totally blind or blind in one eye. Disorders of the digestive tract occupied a prominent place among the diseases coincident with xerophthalmia, and it is probable that inadequate resorption and insufficient diet play an important part in the pathogenesis of xerophthalmia. Feeding with sweetened skimmed milk was responsible for two thirds of the total number of cases of xerophthalmia in children less than 2 years old. An advanced state of dystrophy existed in 75 per cent of the children with xerophthalmia. The vitamin A content of the blood was lower in children with xerophthalmia than in those without it. Vitamin A and the continued oral administration of cod liver oil is recommended for the treatment of xerophthalmia, particularly during the early stages. Prophylaxis is more important than treatment; it should be directed toward improvement of the nutrition of the natives, particularly of children of the preschool age.

Acta Radiologica, Stockholm

21:119-230 (April 30) 1940. **Partial Index**

Half-Axial Projection in Accentuated Lordosis for Roentgen Studies of the Lungs. K. Lindblom.—p. 119.
Bone Defects in Terminal Phalanges. N. Frostberg.—p. 126.
Polyostotic Fibrous Dysplasia. T. Denstad.—p. 143.
Diagnosis and Roentgen Treatment of Certain Forms of Lumbago. C. I. Baastrup.—p. 151.
Myeloscopic and Myelographic Aspects of Posterior Protrusions of Intervertebral Disk Causing Sciatica. W. G. Deucher.—p. 164.
*Comparison Between Roentgenologic and Operative Findings in Acute, Mechanical Ileus. S. A. Chrom.—p. 182.
Studies on Liberation of Sulfuric Acids from Granules of Mast Cells in Subcutaneous Connective Tissue After Exposure to Roentgen and Gamma Rays. B. Sylvén.—p. 206.

Roentgenologic and Surgical Aspects in Ileus.—Chrom evaluates the diagnostic value of roentgenoscopy in cases of acute mechanical ileus on the basis of thirty-two patients admitted to the State Hospital in Copenhagen during the years 1935 to 1938 inclusive. In nineteen of the cases the x-ray examination was made within one hour before the abdomen was opened. In sixteen of these the condition seen on operation agreed with those seen in the x-ray examination, the latter having shown distention of the small intestine alone in eight cases, of the colon alone in five and of both the small intestine and the colon in three. In the remaining three cases the surgical and x-ray observations did not agree. The author concludes that it is generally possible to obtain information regarding the localization of bowel distention by means of x-ray examination of the abdomen without the use of a contrast medium. Fluid levels were present in the roentgenograms in the majority of the cases of surgically verified ileus of the small intestine and in all cases of ileus of the large intestine. Roentgenograms of the abdomen made without a contrast medium do not, however, furnish precise information about the cause, nature and localization of ileus of the small intestine. In these cases judgment must be based chiefly on the history and clinical manifestations, for although the administration of contrast medium by mouth may provide more exact information it will be contraindicated or impossible to carry out in the majority of cases. The situation is quite different in cases of ileus of the large intestine, because here a contrast enema makes it possible to localize the site of obstruction. The author was able to prove this in all twelve cases of mechanical ileus of the colon. A contrast enema was given to nine patients with ileus of the small intestine and the impression was gained that the subsequent roentgenoscopy consitutes a valuable diagnostic aid because it may determine that the obstruction is not in the colon, but it may localize the obstruction and in many cases determine its nature.

Ugeskrift for Læger, Copenhagen

102:255-286 (March 21) 1940

*Frequency of Disk Prolapse as Cause of Sciatica. T. Andersen.—p. 255.
Apparatus for Oxygen Treatment in Cases of Lung Gas Poisoning. O. Bang.—p. 268.
Emergency Mask for Oxygen Treatment in Cases of Phosgene Poisoning. A. Eldahl and M. Vermehren.—p. 274.

Prolapse of a Disk as a Cause of Sciatica.—Andersen made myelographic examinations in eight cases of severe sciatic neuritis in which other methods of examination (gynecologic examination, rectal exploration, roentgen examination of the vertebral column and pelvis) had failed to explain the symptoms. In all the cases myelography showed defects in the contrast shadow which agreed with the symptoms. Operation, done in three of the cases, revealed the prolapse of two disks in one, prolapse of a disk with thickened ligamentum flavum in one and both prolapse of a disk and thickened ligamentum flavum in one. The observations at operation corresponded closely with the results of myelography. The remaining five cases were believed to present similar disorders. Attention is called to the similarity between the classic picture of sciatica and the typical picture of prolapse of an intravertebral disk or thickened ligamentum flavum in the lower lumbar column. The author concludes that apparently idiopathic sciatic "neuritis" probably most often depends on intraspinal disorders, first of all prolapse of a disk or thickening of ligamentum flavum. He advises myelography only on patients so disabled that operative treatment is to be recommended if the results of myelography testify to an intraspinal lesion. In the great majority of cases treatment should be conservative, he says. These lesions of the vertebral column do not always cause sciatica. The symptoms depend on where in the spinal canal the prolapse of the disk or ligamental thickening is located.

102:349-384 (April 11) 1940

*Lines of Guidance in Roentgen Therapy of Leukoses. C. Krebs and J. Bichel.—p. 349.
Methylene Blue as Means Against Methemoglobinemia During Treatment with Chemotherapeutics of Sulfanilamide Group. J. L. Hansen.—p. 352.

Lines of Guidance in Roentgen Therapy of Leukoses.—Krebs and Bichel state that the best treatment for myeloid and lymphatic chronic leukoses is irradiation which can be supplemented by other means, especially treatment with arsenic. Therapy must be individualized. The aim should be as good a general condition as possible without regard to changes in the leukocyte values. The authors emphasize especially that the absolute leukocyte count plays a subordinate role in relation to the qualitative composition of the white blood picture. Roentgen therapy should be interrupted when subjective improvement has set in, even if the leukocyte count is still high. Relative increase in the number of immature forms in the blood picture contraindicates continued therapy. Complete blood examinations twice a week, and frequently more often, are necessary during treatment. The tolerance to roentgen therapy varies greatly, consequently treatment should in all cases begin with small doses.